Jan Delaval

Access DB# 136905

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: S. Kumar Examiner # : 69591 Date: 11/2/04
Art Unit: 1621 Phone Number 30 2-0640 Serial Number: 10/533,442
Mail Box and Bldg/Room Location: REM 5C02 5C18 Results Format Preferred (circle): PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

****

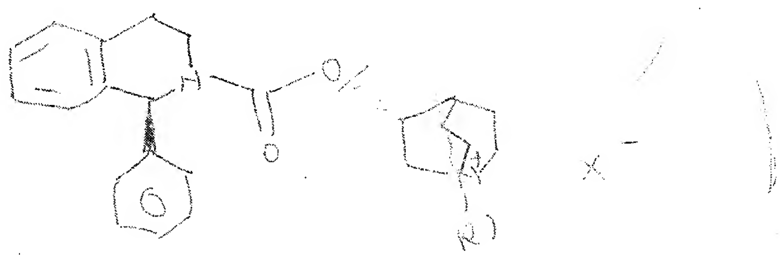
Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Quaternary Ammonium compounds

Inventors (please provide full names): John Gregory Slatter

Earliest Priority Filing Date: 10/29/02

****For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.***



R¹ is alkyl, CH₂-(alkenyl), CH₂-alkynyl, optionally substituted.

(STIC) NOV 2 2004

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STAFF USE ONLY		**Type of Search**		**Vendors and cost where applicable**	
Searcher:	Jan	NA Sequence (#)		STN	✓
Searcher Phone #:	22504	AA Sequence (#)		Dialog	
Searcher Location:		Structure (#)	✓	Questel/Orbit	
Date Searcher Picked Up:	11/3	Bibliographic		Dr.Link	
Date Completed:	11/3	Litigation		Lexis/Nexis	
Searcher Prep & Review Time:		Fulltext		Sequence Systems	
Clerical Prep Time:	40	Patent Family		WWW/Internet	
Online Time:	+10	Other		Other (specify)	

PTO-1590 (8-01)

STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 136905

TO: Shailendra Kumar
Location: 5c03 / 5c18
Wednesday, November 03, 2004
Art Unit: 1621
Phone: 272-0640
Serial Number: 10 / 688442

From: Jan Delaval
Location: Biotech-Chem Library
Rem 1A51
Phone: 272-2504

jan.delaval@uspto.gov

Search Notes

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=> fil reg
FILE 'REGISTRY' ENTERED AT 09:20:08 ON 03 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:     1 NOV 2004  HIGHEST RN 773835-43-1
DICTIONARY FILE UPDATES:    1 NOV 2004  HIGHEST RN 773835-43-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d sta que l6
L1                STR
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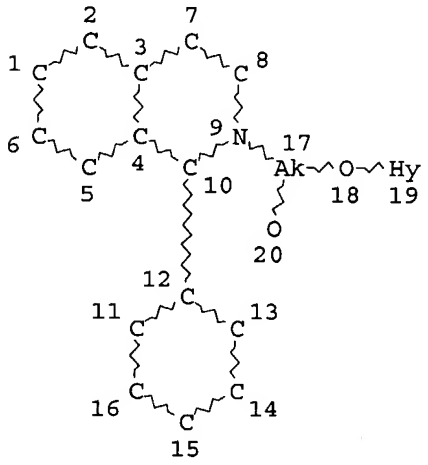


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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  20

STEREO ATTRIBUTES: NONE
L5            24 SEA FILE=REGISTRY SSS FUL L1
L6            23 SEA FILE=REGISTRY ABB=ON  PLU=ON  L5 AND NC5-NC5/ES


=> d ide can tot l6

L6   ANSWER 1 OF 23  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   740780-79-4  REGISTRY
CN   2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,
     1-azabicyclo[2.2.2]oct-3-yl ester, [R-(R*,R*)]- (9CI)  (CA INDEX NAME)
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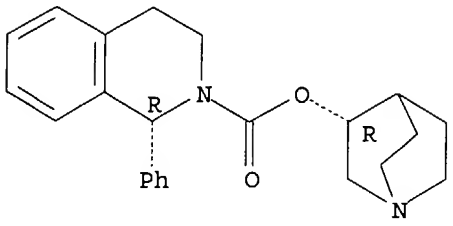
FS STEREOSEARCH
MF C23 H26 N2 O2
CI COM
SR CA

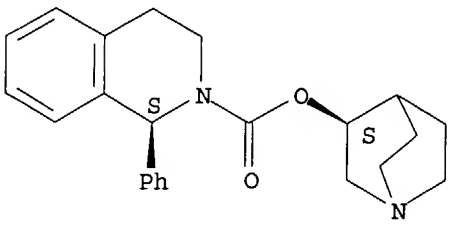
Absolute stereochemistry. Rotation (-).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 ANSWER 2 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 732228-02-3 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H26 N2 O2
CI COM
SR CA

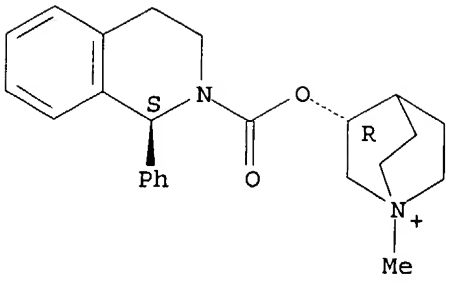
Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 ANSWER 3 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 686745-68-6 REGISTRY
CN 1-Azoniabicyclo[2.2.2]octane, 3-[[[(1S)-3,4-dihydro-1-phenyl-2(1H)-isoquinolinyl]carbonyl]oxy]-1-methyl-, (3R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H29 N2 O2
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)

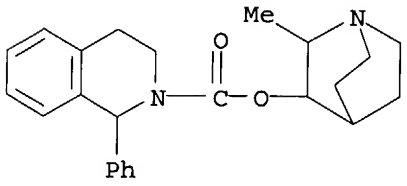
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:391393

L6 ANSWER 4 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 605696-17-1 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 2-methyl-1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Methylquinuclidin-3-yl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate
FS 3D CONCORD
MF C24 H28 N2 O2
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



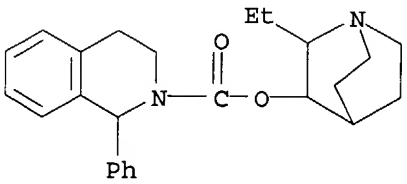
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:277051

L6 ANSWER 5 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 605696-10-4 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 2-ethyl-1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Ethylquinuclidin-3-yl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate
FS 3D CONCORD
MF C25 H30 N2 O2
SR CA
LC STN Files: CA, CAPLUS

DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

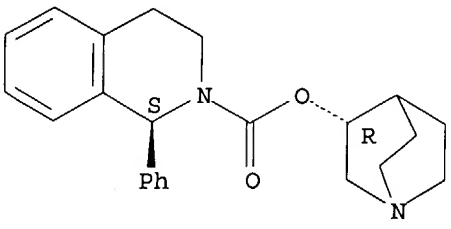
REFERENCE 1: 139:277051

L6 ANSWER 6 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 586349-90-8 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)-, mononitrate (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H26 N2 O2 . H N O3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

CM 1

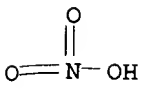
CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7697-37-2
CMF H N O3



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

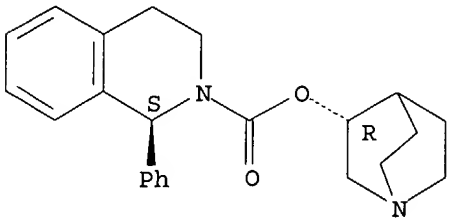
REFERENCE 1: 139:214237

L6 ANSWER 7 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 242478-38-2 REGISTRY
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)-, butanedioate (1:1) (9CI)
OTHER NAMES:
CN Solifenacin succinate
CN YM 905
FS STEREOSEARCH
MF C23 H26 N2 O2 . C4 H6 O4
SR US Adopted Names Council (USAN)
LC STN Files: ADISINSIGHT, BIOSIS, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, IPA, PHAR, PROUSDDR, SYNTHLINE, TOXCENTER, USAN, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

14 REFERENCES IN FILE CA (1907 TO DATE)
14 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:218779

REFERENCE 2: 141:59716

REFERENCE 3: 141:47257

REFERENCE 4: 140:281200

REFERENCE 5: 140:157408

REFERENCE 6: 140:31512

REFERENCE 7: 139:235463

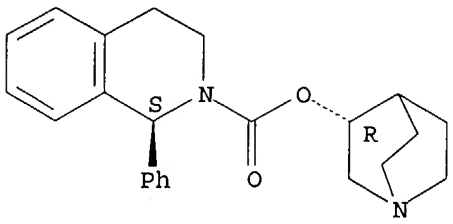
REFERENCE 8: 139:207821

REFERENCE 9: 138:198423

REFERENCE 10: 137:163148

L6 ANSWER 8 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 242478-37-1 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN Solifenacin
FS STEREOSEARCH
MF C23 H26 N2 O2
CI COM
SR US Adopted Names Council (USAN)
LC STN Files: BIOSIS, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, IPA, PHAR, TOXCENTER, USAN, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)
RL.NP Roles from non-patents: BIOL (Biological study); USES (Uses)

Absolute stereochemistry. Rotation (+).



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

10 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
10 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 141:306930

REFERENCE 2: 141:289061

REFERENCE 3: 141:134132

REFERENCE 4: 141:133450

REFERENCE 5: 140:391393

REFERENCE 6: 140:349942

REFERENCE 7: 140:13084

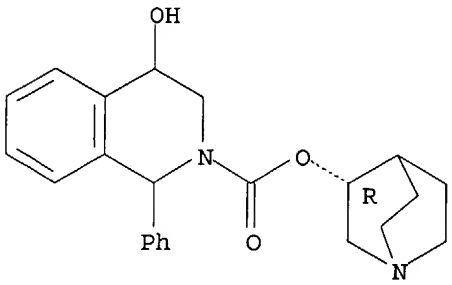
REFERENCE 8: 138:198423

REFERENCE 9: 136:299715

REFERENCE 10: 133:317413

L6 ANSWER 9 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 201660-36-8 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-4-hydroxy-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, [2(R)]-[partial]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H26 N2 O3
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry.



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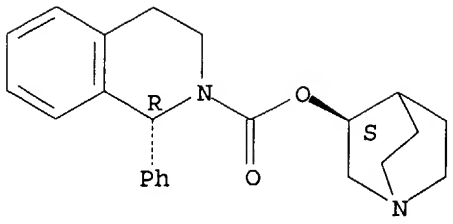
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:114881

L6 ANSWER 10 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180468-40-0 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H26 N2 O2 . Cl H
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

Absolute stereochemistry. Rotation (-).



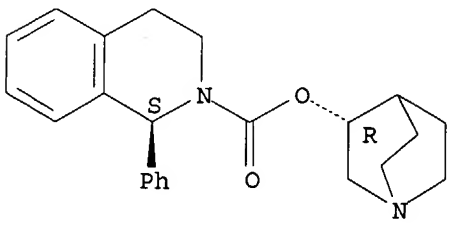
● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 11 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180468-39-7 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H26 N2 O2 . Cl H
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, EMBASE, IMSPATENTS, IMSRESEARCH, IPA, PROUSDDR, SYNTHLINE, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (242478-37-1)

Absolute stereochemistry. Rotation (+).



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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 12 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180468-38-6 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H26 N2 O2 . Cl H

SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, USPATFULL
DT.CA CAplus document type: Patent
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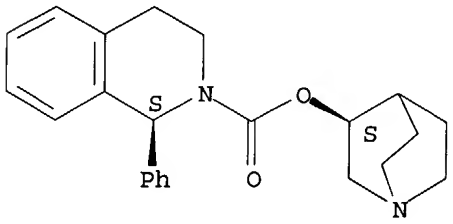
CRN (732228-02-3)

Absolute stereochemistry. Rotation (+).



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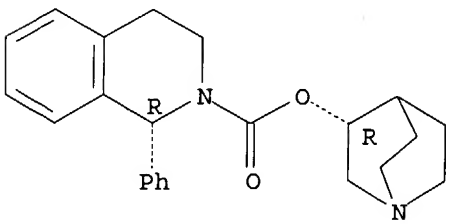
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 13 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180468-37-5 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R*,R*)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H26 N2 O2 . Cl H
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (740780-79-4)

Absolute stereochemistry. Rotation (-).



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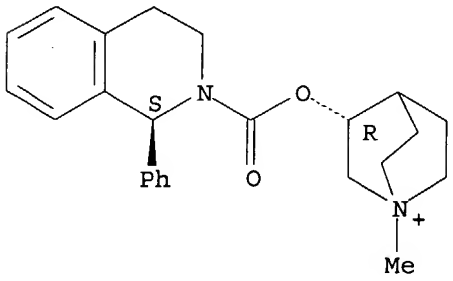
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 14 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-29-1 REGISTRY
CN 1-Azoniabicyclo[2.2.2]octane, 3-[[[(1S)-3,4-dihydro-1-phenyl-2(1H)-isoquinolinyl]carbonyl]oxy]-1-methyl-, iodide, (3R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H29 N2 O2 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (686745-68-6)

Absolute stereochemistry.



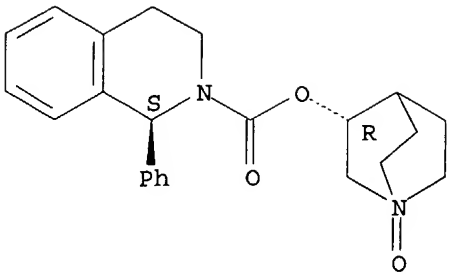
● I^-

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 15 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-28-0 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-oxido-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H26 N2 O3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

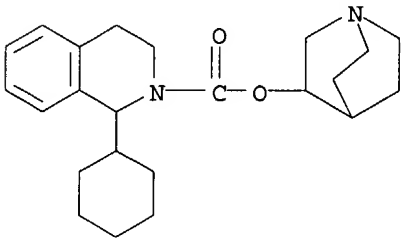
Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 16 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-27-9 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 1-cyclohexyl-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)
MF C23 H32 N2 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

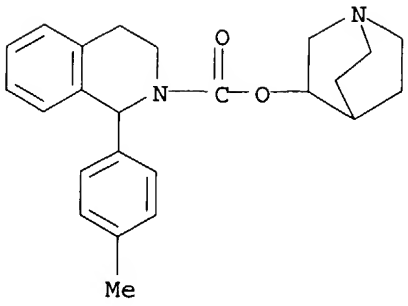


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 17 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-25-7 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(4-methylphenyl)-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C24 H28 N2 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

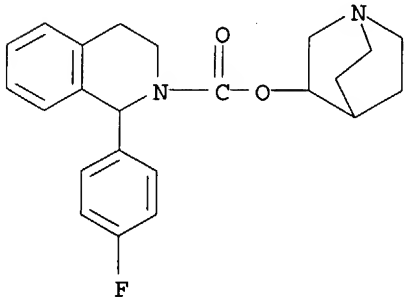


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 18 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-24-6 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-fluorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H25 F N2 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

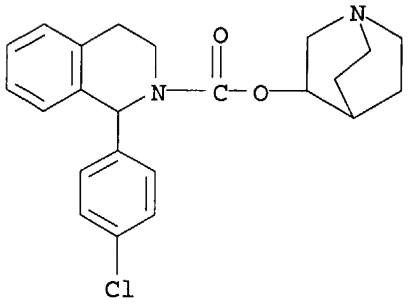
REFERENCE 1: 125:167804

L6 ANSWER 19 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-23-5 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-chlorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-chlorophenyl)-3,4-dihydro-,

1-azabicyclo[2.2.2]oct-3-yl ester, (E)-2-butenedioate (1:1)
FS STEREOSEARCH
MF C23 H25 Cl N2 O2 . C4 H4 O4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

CM 1

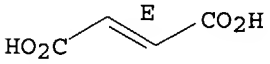
CRN 180272-22-4
CMF C23 H25 Cl N2 O2



CM 2

CRN 110-17-8
CMF C4 H4 O4

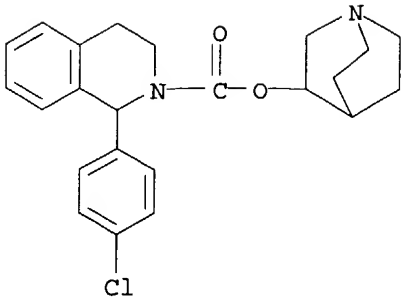
Double bond geometry as shown.



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

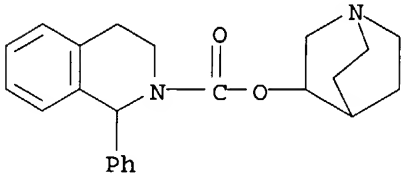
REFERENCE 1: 125:167804

L6 ANSWER 20 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-22-4 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-chlorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H25 Cl N2 O2
CI COM
SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L6 ANSWER 21 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-16-6 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride (9CI) (CA INDEX NAME)
MF C23 H26 N2 O2 . Cl H
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, EMBASE, IMSPATENTS, IMSRESEARCH, PROUSDDR, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
CRN (180272-14-4)



● HCl

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 125:167804

L6 ANSWER 22 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-15-5 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)
MF C23 H26 N2 O2 . C2 H2 O4
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, IMSPATENTS, IMSRESEARCH, PROUSDDR, USPATFULL
DT.CA CAplus document type: Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); USES (Uses)

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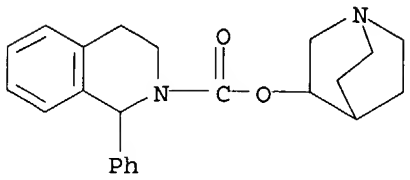
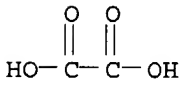
CRN 180272-14-4
CMF C23 H26 N2 O2



CM 2

CRN 144-62-7
CMF C2 H2 O4

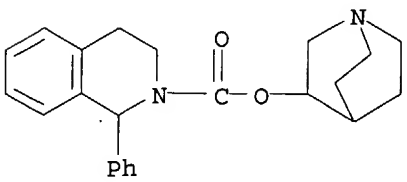


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 132:202452

REFERENCE 2: 125:167804

L6 ANSWER 23 OF 23 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180272-14-4 REGISTRY
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C23 H26 N2 O2
CI COM
SR CA
LC STN Files: ADISINSIGHT, CA, CAPLUS, EMBASE, IMSPATENTS, IMSRESEARCH, PROUSDDR, SYNTHLINE, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); USES (Uses)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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               3 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
               3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE   1:  140:31512

REFERENCE   2:  138:100946

REFERENCE   3:  125:167804


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               SET COST OFF

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L3               STR L1
L4             0 S L3
L5            24 S L1 FUL
               SAV L5 KUMAR688/A
L6            23 S L5 AND NC5-NC5/ES

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L7             0 S L6

     FILE 'HCAPLUS' ENTERED AT 09:18:19 ON 03 NOV 2004
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L9             1 S L8 AND (US20040138253/PN OR (US2003-688442# OR US2002-421951#
L10            1 S L8 AND SLATTER J?/AU
L11            3 S L8 AND (PHARMACIA? OR UPJOHN?)/PA,CS
L12            3 S L9-L11
L13           18 S L8 AND (PD<=20021029 OR PRD<=20021029 OR AD<=20021029)
L14           19 S L12,L13

     FILE 'USPATFULL' ENTERED AT 09:19:53 ON 03 NOV 2004
L15            6 S L8

     FILE 'REGISTRY' ENTERED AT 09:20:08 ON 03 NOV 2004

=> fil uspatfull
FILE 'USPATFULL' ENTERED AT 09:20:28 ON 03 NOV 2004
CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE COVERS 1971 TO PATENT PUBLICATION DATE: 2 Nov 2004 (20041102/PD)
FILE LAST UPDATED: 2 Nov 2004 (20041102/ED)
HIGHEST GRANTED PATENT NUMBER: US6813778
HIGHEST APPLICATION PUBLICATION NUMBER: US2004216205
CA INDEXING IS CURRENT THROUGH 2 Nov 2004 (20041102/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 2 Nov 2004 (20041102/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Aug 2004
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Aug 2004

>>>  USPAT2 is now available.  USPATFULL contains full text of the     <<<
>>>  original, i.e., the earliest published granted patents or         <<<
>>>  applications.  USPAT2 contains full text of the latest US         <<<
>>>  publications, starting in 2001, for the inventions covered in     <<<
>>>  USPATFULL.  A USPATFULL record contains not only the original     <<<
>>>  published document but also a list of any subsequent              <<<
>>>  publications.  The publication number, patent kind code, and      <<<
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>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

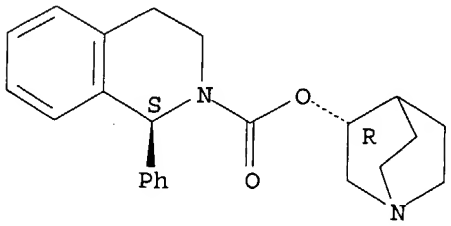
=> d l15 bib abs hitstr tot

L15 ANSWER 1 OF 6 USPATFULL on STN
AN 2004:255292 USPATFULL
TI Methods for treating lower urinary tract disorders using alpha2delta subunit calcium channel modulators with smooth muscle modulators
IN Fraser, Matthew Oliver, Apex, NC, UNITED STATES
Thor, Karl Bruce, Morrisville, NC, UNITED STATES
Burgard, Edward C., Chapel Hill, NC, UNITED STATES
Brettman, Lee R., Sudbury, MA, UNITED STATES
Landau, Steven B., Wellesley, MA, UNITED STATES
Ricca, Daniel J., Rougemont, NC, UNITED STATES
PA Dynogen Pharmacueticals, Inc., Boston, MA, UNITED STATES (U.S. corporation)
PI US 2004198822 A1 20041007
AI US 2004-805977 A1 20040322 (10)
PRAI US 2003-456835P 20030321 (60)
US 2003-486148P 20030710 (60)
US 2003-509570P 20031008 (60)
US 2004-534871P 20040108 (60)
US 2004-548250P 20040227 (60)
DT Utility
FS APPLICATION
LREP ALSTON & BIRD LLP, BANK OF AMERICA PLAZA, 101 SOUTH TRYON STREET, SUITE 4000, CHARLOTTE, NC, 28280-4000
CLMN Number of Claims: 43
ECL Exemplary Claim: 1
DRWN 23 Drawing Page(s)
LN.CNT 4835
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is provided for using α.sub.2δ subunit calcium channel modulators or other compounds that interact with the α.sub.2δ calcium channel subunit in combination with one or more compounds with smooth muscle modulatory effects to treat and/or alleviate the symptoms associated with painful and non-painful lower urinary tract disorders in normal and spinal cord injured patients. According to the present invention, α.sub.2δ subunit calcium channel modulators include GABA analogs (e.g. gabapentin and pregabalin), fused bicyclic or tricyclic amino acid analogs of gabapentin, and amino acid compounds. Compounds with smooth muscle modulatory effects include antimuscarinics, β3 adrenergic agonists, spasmolytics, neurokinin receptor antagonists, bradykinin receptor antagonists, and nitric oxide donors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **242478-37-1**, Solifenacin
(methods for treating lower urinary tract disorders using smooth muscle

modulators and alpha-2-delta subunit calcium channel modulators)
RN 242478-37-1 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

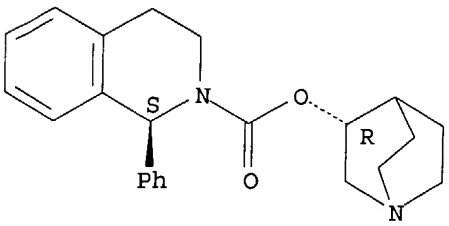
Absolute stereochemistry. Rotation (+).



L15 ANSWER 2 OF 6 USPATFULL on STN
AN 2004:179083 USPATFULL
TI Quaternary ammonium compounds
IN Slatter, John Gregory, Bellevue, WA, UNITED STATES
PI US 2004138253 A1 20040715
AI US 2003-688442 A1 20031017 (10)
PRAI US 2002-421951P 20021029 (60)
DT Utility
FS APPLICATION
LREP PHARMACIA & UPJOHN, 301 HENRIETTA ST, 0228-32-LAW, KALAMAZOO, MI, 49007
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 388
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention features quaternary ammonium compounds of formula I, described herein, and their use in treating asthma, chronic obstructive pulmonary disorder, allergic rhinitis, and infectious rhinitis.

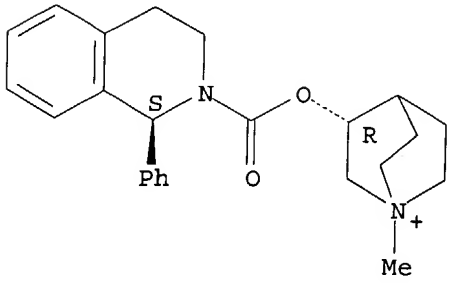
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **242478-37-1D**, quaternary ammonium salts **686745-68-6D**, halide salts
(preparation of quaternary ammonium quinuclidinium derivs. as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disease, and allergic and infectious rhinitis)
RN 242478-37-1 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



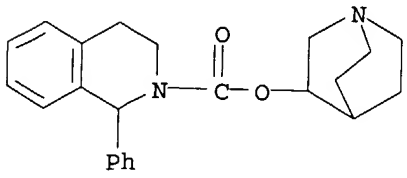
RN 686745-68-6 USPATFULL
CN 1-Azoniabicyclo[2.2.2]octane, 3-[[[(1S)-3,4-dihydro-1-phenyl-2(1H)-isoquinolinyl]carbonyl]oxy]-1-methyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

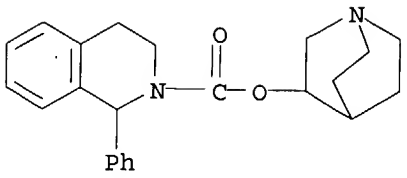


L15 ANSWER 3 OF 6 USPATFULL on STN
AN 2004:179082 USPATFULL
TI Pharmaceutical composition for therapy of interstitial cystitis
IN Ikeda, Ken, Tsukuba-shi Ibaraki, JAPAN
Takeuchi, Makoto, Tsukuba-shi Ibaraki, JAPAN
PI US 2004138252 A1 20040715
AI US 2003-479798 A1 20031205 (10)
WO 2002-JP6904 20020708
PRAI JP 2001-209041 20010710
DT Utility
FS APPLICATION
LREP Finnegan Henderson Farabow, Garrett & Dunner, 1300 I Street NW, Washington, DC, 20005-3315
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 1 Drawing Page(s)
LN.CNT 371
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A depressant of capsaicin-sensitive sensory nerve, containing quinuclidin-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate or a salt thereof as an active ingredient, specifically a therapeutic drug of interstitial cystitis, hypersensitive disorder of the lower urinary tract, and/or abacterial prostatitis.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **180272-14-4 180272-14-4D**, salts
(quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)
RN 180272-14-4 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-14-4 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



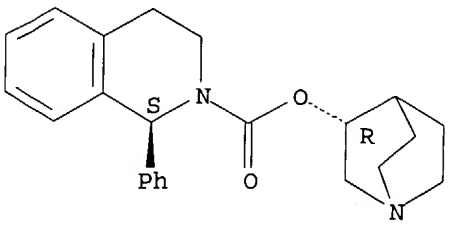
L15 ANSWER 4 OF 6 USPATFULL on STN
AN 2003:271564 USPATFULL
TI Method of using cyclooxygenase inhibitors and antimuscarinic agents
IN Versi, Ebrahim, Gladstone, NJ, UNITED STATES
PI US 2003191172 A1 20031009
AI US 2003-368091 A1 20030218 (10)
PRAI US 2002-357888P 20020219 (60)
DT Utility
FS APPLICATION
LREP Pharmacia Corporation, Global Patent Department, PO Box 1027, St. Louis, MO, 63006
CLMN Number of Claims: 48
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1067
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method for the use of a cyclooxygenase-2 inhibitor, alone or in combination with an anti-muscarinic agent, for the treatment or prophylaxis of a urinary incontinence condition in a subject in need of such treatment or prevention, comprising administering to the subject an effective amount of the cyclooxygenase-2 inhibitor and, optionally, the anti-muscarinic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **242478-38-2**, YM-905
(cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)
RN 242478-38-2 USPATFULL
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

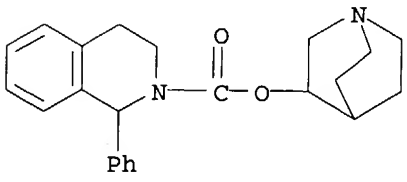
CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

L15 ANSWER 5 OF 6 USPATFULL on STN
AN 2001:8062 USPATFULL
TI Quinuclidine derivatives and medicinal composition thereof
IN Takeuchi, Makoto, Ibaraki, Japan
Naito, Ryo, Ibaraki, Japan
Hayakawa, Masahiko, Ibaraki, Japan
Okamoto, Yoshinori, Ibaraki, Japan
Yonetoku, Yasuhiro, Ibaraki, Japan
Ikeda, Ken, Chiba, Japan
Isomura, Yasuo, Ibaraki, Japan
PA Yamanouchi Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)
PI US 6174896 B1 20010116
AI US 1999-312392 19990514 (9)
RLI Continuation of Ser. No. US 860377, now patented, Pat. No. US 6017927
PRAI JP 1994-327045 19941228
DT Utility
FS Granted
EXNAM Primary Examiner: Morris, Patricia L.
LREP Sughrue, Mion, Zinn, Macpeak & Seas, PLLC
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1368
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Quinuclidine derivatives represented by general following general formula (I), salts, N-oxides or quaternary ammonium salts thereof, and medicinal compositions containing the same. ##STR1##

The compound has an antagonistic effect on muscarinic M.sub.3 receptors and is useful as a preventive or remedy for urologic diseases, respiratory diseases or digestive diseases.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **180272-14-4P 180272-15-5P 180272-16-6P**
180272-23-5P 180272-24-6P 180272-25-7P
180272-27-9P 180272-28-0P 180272-29-1P
180468-37-5P 180468-38-6P 180468-39-7P
180468-40-0P
(preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)
RN 180272-14-4 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)

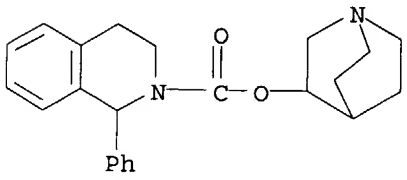


RN 180272-15-5 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-,

1-azabicyclo[2.2.2]oct-3-yl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)

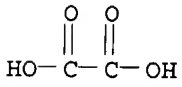
CM 1

CRN 180272-14-4
CMF C23 H26 N2 O2

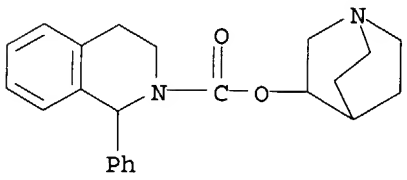


CM 2

CRN 144-62-7
CMF C2 H2 O4



RN 180272-16-6 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

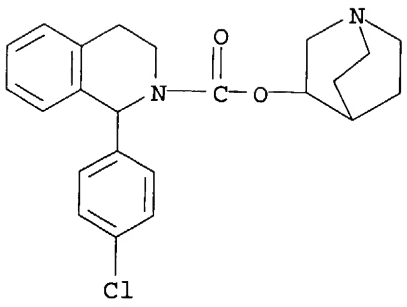


● HCl

RN 180272-23-5 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-chlorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

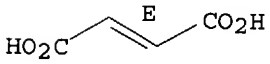
CRN 180272-22-4
CMF C23 H25 Cl N2 O2



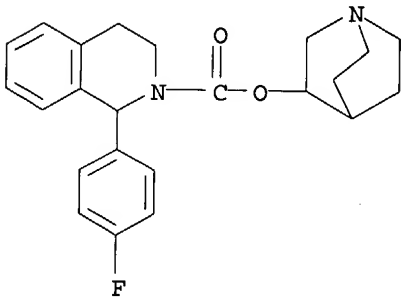
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

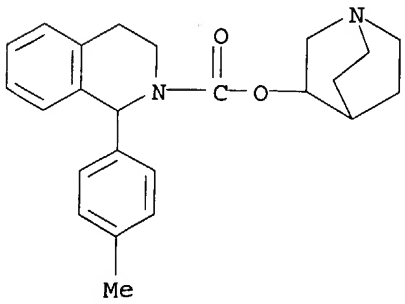
Double bond geometry as shown.



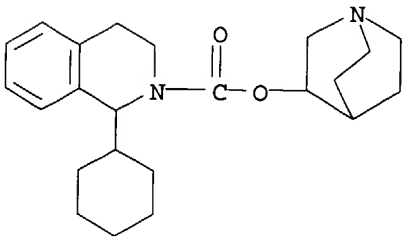
RN 180272-24-6 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-fluorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-25-7 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(4-methylphenyl)-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)

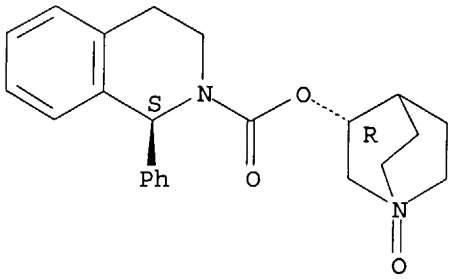


RN 180272-27-9 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 1-cyclohexyl-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



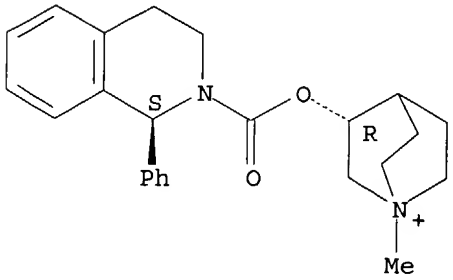
RN 180272-28-0 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-oxido-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180272-29-1 USPATFULL
CN 1-Azoniabicyclo[2.2.2]octane, 3-[[[(1S)-3,4-dihydro-1-phenyl-2(1H)-isoquinolinyl]carbonyl]oxy]-1-methyl-, iodide, (3R)- (9CI) (CA INDEX NAME)

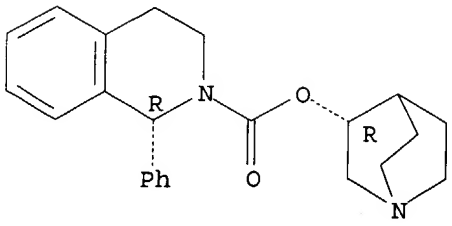
Absolute stereochemistry.



● I^-

RN 180468-37-5 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

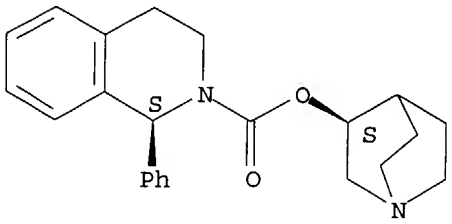
Absolute stereochemistry. Rotation (-).



● HCl

RN 180468-38-6 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

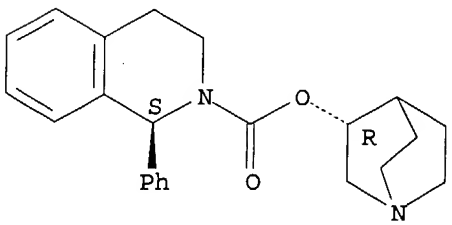
Absolute stereochemistry. Rotation (+).



● HCl

RN 180468-39-7 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

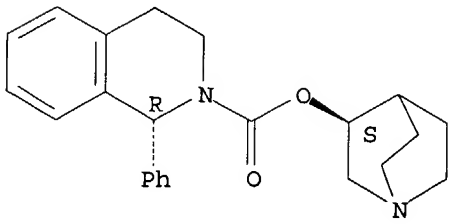
Absolute stereochemistry. Rotation (+).



● HCl

RN 180468-40-0 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

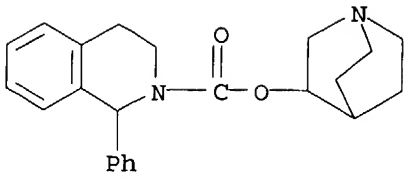
Absolute stereochemistry. Rotation (-).



● HCl

L15 ANSWER 6 OF 6 USPATFULL on STN
AN 2000:9916 USPATFULL
TI Quinuclidine derivatives and medicinal composition thereof
IN Takeuchi, Makoto, Ibaraki, Japan
Naito, Ryo, Ibaraki, Japan
Hayakawa, Masahiko, Ibaraki, Japan
Okamoto, Yoshinori, Ibaraki, Japan
Yonetoku, Yasuhiro, Ibaraki, Japan
Ikeda, Ken, Chiba, Japan
Isomura, Yasuo, Ibaraki, Japan
PA Yamanouchi Pharmaceutical Co., Ltd., Tokyo, Japan (non-U.S. corporation)
PI US 6017927 20000125
WO 9620194 19960704
AI US 1997-860377 19970828 (8)
WO 1995-JP2713 19951227
19970828 PCT 371 date
19970828 PCT 102(e) date
PRAI JP 1994-327045 19941228
DT Utility
FS Granted
EXNAM Primary Examiner: Morris, Patricia L.
LREP Sughrue, Mion, Zinn, Macpeak & Seas, PLLC
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1526
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Quinuclidine derivatives represented by general following general formula (I), salts, N-oxides or quaternary ammonium salts thereof, and medicinal compositions containing the same. ##STR1## The compound has an antagonistic effect on muscarinic M.sub.3 receptors and is useful as a preventive or remedy for urologic diseases, respiratory diseases or digestive diseases.

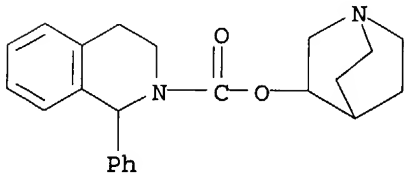
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
IT **180272-14-4P 180272-15-5P 180272-16-6P**
180272-23-5P 180272-24-6P 180272-25-7P
180272-27-9P 180272-28-0P 180272-29-1P
180468-37-5P 180468-38-6P 180468-39-7P
180468-40-0P
(preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)
RN 180272-14-4 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-15-5 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)

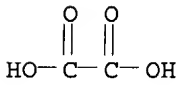
CM 1

CRN 180272-14-4
CMF C23 H26 N2 O2

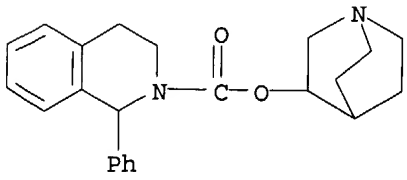


CM 2

CRN 144-62-7
CMF C2 H2 O4



RN 180272-16-6 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

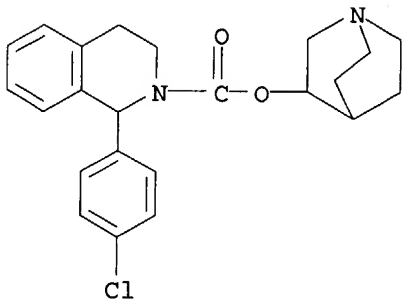


● HCl

RN 180272-23-5 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-chlorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

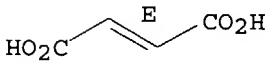
CRN 180272-22-4
CMF C23 H25 Cl N2 O2



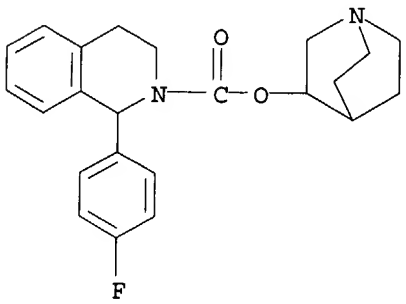
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

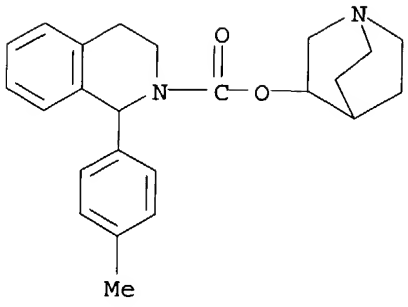
Double bond geometry as shown.



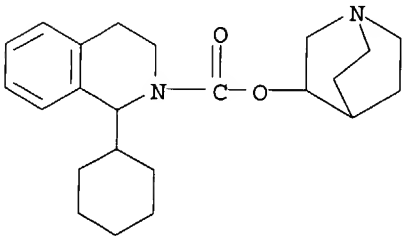
RN 180272-24-6 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-fluorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-25-7 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(4-methylphenyl)-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)

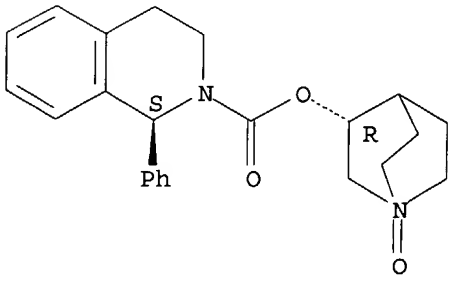


RN 180272-27-9 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 1-cyclohexyl-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



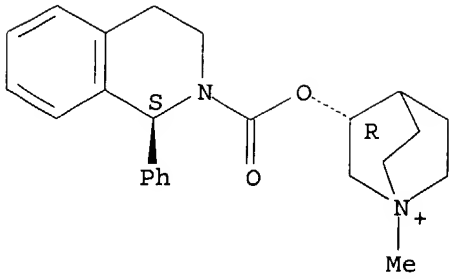
RN 180272-28-0 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-oxido-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180272-29-1 USPATFULL
CN 1-Azoniabicyclo[2.2.2]octane, 3-[[[(1S)-3,4-dihydro-1-phenyl-2(1H)-isoquinolinyl]carbonyl]oxy]-1-methyl-, iodide, (3R)- (9CI) (CA INDEX NAME)

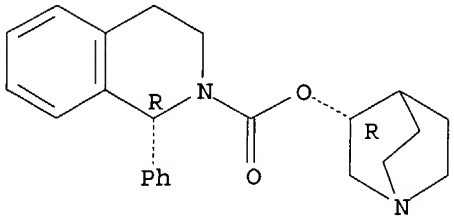
Absolute stereochemistry.



● I^-

RN 180468-37-5 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

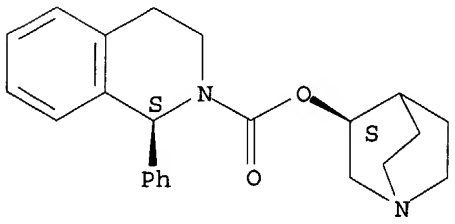
Absolute stereochemistry. Rotation (-).



● HCl

RN 180468-38-6 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

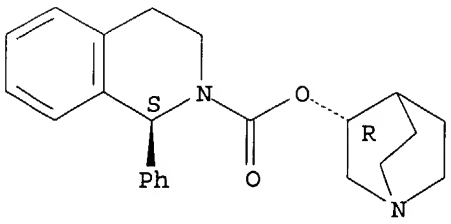
Absolute stereochemistry. Rotation (+).



● HCl

RN 180468-39-7 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

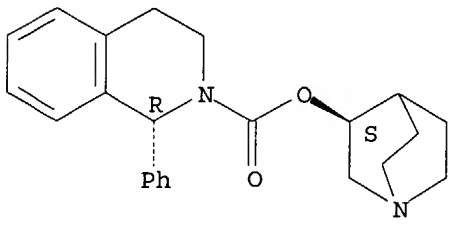
Absolute stereochemistry. Rotation (+).



● HCl

RN 180468-40-0 USPATFULL
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 09:20:41 ON 03 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 3 Nov 2004 VOL 141 ISS 19
FILE LAST UPDATED: 1 Nov 2004 (20041101/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> d l14 all hitstr tot

L14  ANSWER 1 OF 19  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:633513  HCAPLUS
DN   141:134132
ED   Entered STN:  06 Aug 2004
TI   Reduced dose of tolterodine and other antimuscarinic agents for treating
     urinary disorders
IN   Korberly, Barbara H.; Danehower, Susan M.
PA   Pharmacia AB, Swed.
SO   PCT Int. Appl., 21 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  A61K031-135
     ICS  A61P013-10; A61K031-216; A61K031-4025; A61K031-439
CC   1-12 (Pharmacology)
     Section cross-reference(s): 63
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.          DATE
     ---------------     ----   --------    --------------------     --------
PI   WO 2004064821        A1    20040805    WO 2004-IB169            20040114
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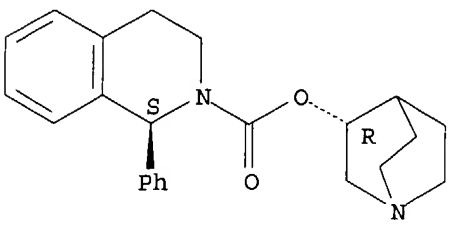
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
PRAI US 2003-441690P      P     20030122
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------   -----  ----------------------------------------------
 WO 2004064821    ICM    A61K031-135
                  ICS    A61P013-10; A61K031-216; A61K031-4025; A61K031-439
AB   The invention discloses a method, preferably an oral method, for treating
     urinary disorders, e.g. unstable or overactive bladder, while minimizing
     the occurrences of dry mouth, dyspepsia and reduced stream of tears.  The
     methods of the invention comprise orally administering to a mammal,
     preferably a human, a pharmaceutically ED of an antimuscarinic agent, such
     as tolterodine, when needed, whereby a symptomatic relief of urgency
     and/or frequency is achieved.
ST   tolterodine bladder disorder adverse effect redn; antimuscarinic agent
     bladder disorder adverse effect redn
IT   Drug delivery systems
        (capsules, controlled-release; tolterodine or other antimuscarinic
        agent dose reduction for treatment of urinary disorders)
IT   Drug delivery systems
        (capsules; tolterodine or other antimuscarinic agent dose reduction for
        treatment of urinary disorders)
IT   Toxicity
        (drug; tolterodine or other antimuscarinic agent dose reduction for
        treatment of urinary disorders)
IT   Drug delivery systems
        (oral; tolterodine or other antimuscarinic agent dose reduction for
        treatment of urinary disorders)
IT   Drug delivery systems
        (tablets, controlled-release; tolterodine or other antimuscarinic agent
        dose reduction for treatment of urinary disorders)
IT   Drug delivery systems
        (tablets; tolterodine or other antimuscarinic agent dose reduction for
        treatment of urinary disorders)
```

IT Bladder, disease
Digestive tract, disease
Human
Muscarinic antagonists
Nervous system, disease
(tolterodine or other antimuscarinic agent dose reduction for treatment of urinary disorders)
IT 5633-20-5, Oxybutynin 124937-51-5, Tolterodine 124937-52-6, Detrol 133099-04-4, Darifenacin **242478-37-1**, Solifenacin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tolterodine or other antimuscarinic agent dose reduction for treatment of urinary disorders)
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Appell, R; UROLOGY 1997, V50, P90 MEDLINE
(2) Jonas, U; WORLD JOURNAL OF UROLOGY 1997, V15(2), P144 HCAPLUS
(3) Nilvebrant, L; PHARMACOLOGY & TOXICOLOGY 1997, V81(4), P169 HCAPLUS
(4) Olsson, B; CLINICAL PHARMACOKINETICS 2001, V40(3), P227 HCAPLUS
(5) Rentzhog, L; BRITISH JOURNAL OF UROLOGY 1998, V81(1), P42 HCAPLUS
(6) Sussman, D; CURRENT MEDICAL RESEARCH AND OPINION 2002, V18(4), P177 HCAPLUS
(7) Toma, H; HINYOKIKA KIYO ACTA UROLOGICA JAPONICA 1986, V32(6), P907 MEDLINE
(8) van Kerrebroeck, P; NEUROUROLOGY AND URODYNAMICS 1998, V17(5), P499 HCAPLUS
(9) van Kerrebroeck, P; UROLOGY 2001, V57(3), P414 MEDLINE
(10) Yamauchi, K; HINYOKIKA KIYO ACTA UROLOGICA JAPONICA 1990, V36(12), P1485 MEDLINE
(11) Yokoyama, E; HINYOKIKA KIYO ACTA UROLOGICA JAPONICA 1990, V36(7), P869 MEDLINE
IT **242478-37-1**, Solifenacin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tolterodine or other antimuscarinic agent dose reduction for treatment of urinary disorders)
RN 242478-37-1 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L14 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:390244 HCAPLUS
DN 140:391393
ED Entered STN: 13 May 2004
TI Quinuclidinium derivatives as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disorder, allergic rhinitis, and infectious rhinitis
IN **Slatter, John Gregory**
PA **Pharmacia & Upjohn Company, USA**
SO PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DT Patent
LA English

IC ICM C07D453-02
ICS A61K031-47; A61P011-00
CC 31-4 (Alkaloids)
Section cross-reference(s): 1, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004039801	A1	20040513	WO 2003-IB4641	20031017 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD

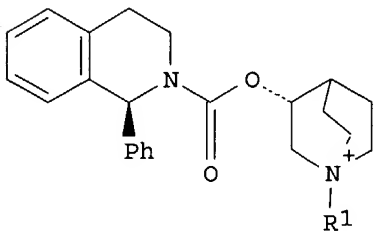
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004138253	A1	20040715	US 2003-688442	20031017 <--
PRAI US 2002-421951P	P	20021029 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004039801	ICM	C07D453-02
	ICS	A61K031-47; A61P011-00

OS MARPAT 140:391393
GI



I

X

AB The invention features quaternary ammonium compds. I (R1 = C1-C6 alkyl, -CH2-(C1-C4 alkenyl), -CH2-(C1-C6 alkynyl); X = I, Br, Cl, or the anion of tartaric, sulfuric, phosphoric, nitric, citric, methanesulfonic, CH3(CH2)nCOOH where n = 0-4, COOH(CH2)nCOOH where n = 1-4, COOHCH:CHCOOH, or benzoic acids) described herein, and their use in treating asthma, chronic obstructive pulmonary disorder, allergic rhinitis, and infectious rhinitis.

ST quinuclidinium quaternary ammonium deriv antimuscarinic agent prepn; asthma allergic infectious rhinitis quinuclidinium quaternary ammonium deriv treatment; chronic obstructive pulmonary disorder quinuclidinium quaternary ammonium deriv treatment

IT Nose, disease
(allergic rhinitis, treatment of; preparation of quaternary ammonium quinuclidinium derivs. as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disease, and allergic and infectious rhinitis)

IT Lung, disease

(chronic obstructive, treatment of; preparation of quaternary ammonium quinuclidinium derivs. as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disease, and allergic and infectious rhinitis)

IT Muscarinic antagonists
(preparation of quaternary ammonium quinuclidinium derivs. as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disease, and allergic and infectious rhinitis)

IT Nose, disease
(rhinitis, treatment of; preparation of quaternary ammonium quinuclidinium derivs. as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disease, and allergic and infectious rhinitis)

IT Asthma
(treatment of; preparation of quaternary ammonium quinuclidinium derivs. as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disease, and allergic and infectious rhinitis)

IT **242478-37-1D**, quaternary ammonium salts **686745-68-6D**, halide salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of quaternary ammonium quinuclidinium derivs. as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disease, and allergic and infectious rhinitis)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Husbands, G; US 5512574 A 1996 HCAPLUS

(2) Stobie, A; US 5292749 A 1994 HCAPLUS

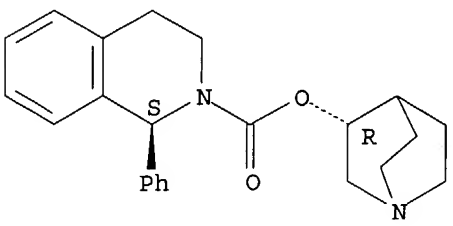
(3) Yamanouchi Pharma Co Ltd; EP 0801067 A 1997 HCAPLUS

IT **242478-37-1D**, quaternary ammonium salts **686745-68-6D**, halide salts
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of quaternary ammonium quinuclidinium derivs. as antimuscarinic agents for the treatment of asthma, chronic obstructive pulmonary disease, and allergic and infectious rhinitis)

RN 242478-37-1 HCAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

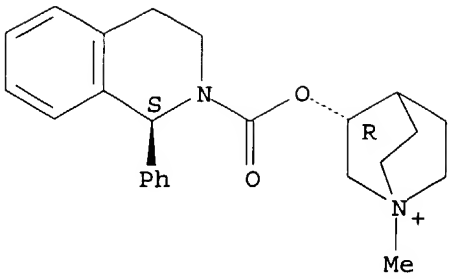
Absolute stereochemistry. Rotation (+).



RN 686745-68-6 HCAPLUS

CN 1-Azoniabicyclo[2.2.2]octane, 3-[[[(1S)-3,4-dihydro-1-phenyl-2(1H)-isoquinolinyl]carbonyl]oxy]-1-methyl-, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:991340 HCAPLUS
DN 140:31512
ED Entered STN: 21 Dec 2003
TI Therapeutic agents for overactive bladder containing tamsulosin
IN Van Meeteren, Rian; Visser, Nico J.; Kajii, Hiroshi; Takiguchi, Nobuyuki
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K031-18
ICS A61K031-4725; A61K045-00; A61P013-00; A61P013-02; A61P013-10; A61P043-00; C07D453-02
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003103659	A1	20031218	WO 2003-JP7149	20030605 <--

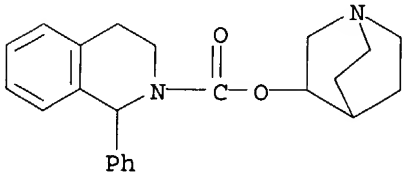
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI JP 2002-166408 A 20020607 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003103659	ICM	A61K031-18
	ICS	A61K031-4725; A61K045-00; A61P013-00; A61P013-02; A61P013-10; A61P043-00; C07D453-02

AB Disclosed is a medicinal composition for treatments for overactive bladder which contains tamsulosin or a pharmaceutically acceptable salt thereof as an active ingredient. A composition containing tamsulosin in combination with a muscarinic receptor antagonist for treatment of overactive bladder is also disclosed. A sustained-release tablet containing tamsulosin hydrochloride 0.5 mg/tablet was prepared, and administered to a patient with overactive bladder.
ST tamsulosin overactive bladder treatment; muscarinic antagonist tamsulosin overactive bladder treatment
IT Drug delivery systems

(capsules; therapeutic agents for overactive bladder containing tamsulosin)
IT Bladder, disease
(incontinence; therapeutic agents for overactive bladder containing tamsulosin)
IT Drug delivery systems
(tablets, sustained-release; therapeutic agents for overactive bladder containing tamsulosin)
IT Human
(therapeutic agents for overactive bladder containing tamsulosin)
IT Muscarinic antagonists
(therapeutic agents for overactive bladder containing tamsulosin and muscarinic antagonists)
IT 106133-20-4, Tamsulosin 106463-17-6, Tamsulosin hydrochloride
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agents for overactive bladder containing tamsulosin)
IT **180272-14-4 242478-38-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agents for overactive bladder containing tamsulosin and muscarinic antagonists)
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Scarpa, R; European Urologry 2001, V40(suppl 4), P12
(2) Sellers, D; World Journal of Urology 2001, V19(5), P307 HCAPLUS
(3) Yamanouchi Pharmaceutical Co Ltd; EP 801067 A1 1997 HCAPLUS
(4) Yamanouchi Pharmaceutical Co Ltd; WO 9620194 A1 1997 HCAPLUS
IT **180272-14-4 242478-38-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic agents for overactive bladder containing tamsulosin and muscarinic antagonists)
RN 180272-14-4 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)

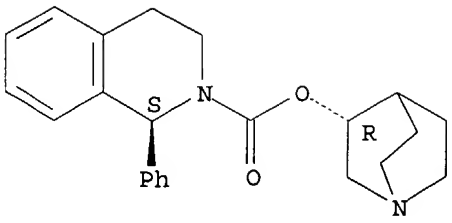


RN 242478-38-2 HCAPLUS
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

L14 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:950829 HCAPLUS
DN 140:13084
ED Entered STN: 07 Dec 2003
TI Combination of selected opioids with other active substances for use in the therapy of urinary incontinence
IN Christoph, Thomas
PA Grunenthal G.m.b.H., Germany
SO PCT Int. Appl., 126 pp.
CODEN: PIXXD2
DT Patent
LA German
IC ICM A61K031-135
ICS A61K031-137; A61K031-485
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003099268	A1	20031204	WO 2003-EP5529	20030527 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10224107	A1	20031211	DE 2002-10224107	20020529 <--
PRAI DE 2002-10224107	A	20020529 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003099268	ICM	A61K031-135
	ICS	A61K031-137; A61K031-485

OS MARPAT 140:13084
AB The invention discloses the use of a combination of opioids (e.g. tramadol) with other active substances for producing a drug for the

treatment of urinary urgency or urinary incontinence. The invention also relates to corresponding medicaments and to a method for treating urinary urgency or urinary incontinence.

ST incontinence urinary treatment opioid drug combination; urinary urge treatment opioid drug combination; tramadol drug combination urinary incontinence urge

IT Bladder, disease
(incontinence; opioid combination with other active substances for treatment of urinary incontinence)

IT Drug delivery systems
(injections; opioid combination with other active substances for treatment of urinary incontinence)

IT Drug delivery systems
(opioid combination with other active substances for treatment of urinary incontinence)

IT Bladder
(urinary urge; opioid combination with other active substances for treatment of urinary incontinence)

IT 57-27-2, * Morphin, biological studies 57-42-1, Pethidine 62-67-9, Nalorphine 76-42-6, Oxycodone 76-57-3, Codeine 76-58-4, Ethylmorphine 77-07-6, Levorphanol 125-28-0, Dihydrocodeine 125-29-1, Hydrocodone 125-58-6, Levomethadone 302-41-0, Piritramide 357-56-2, Dextromoramide 359-83-1, Pentazocine 437-38-7, Fentanyl 466-99-9, Hydromorphone 469-62-5, Dextropropoxyphene 469-79-4, Ketobemidone 561-27-3, Diacetylmorphine 915-30-0, Diphenoxylate 1199-99-1D, derivs. 1477-40-3, Levomethadyl Acetate 14521-96-1, Etorphine 20594-83-6, Nalbuphine 21363-18-8, Viminol 27203-92-5, Tramadol 42408-82-2, Butorphanol 51931-66-9, Tilidine 52485-79-7, Buprenorphine 53648-55-8, Dezocine 54340-58-8, Meptazinol 56030-54-7 71195-58-9, Alfentanyl 80456-81-1, O-Demethyltramadol 132875-61-7, Remifentanyl 138853-73-3
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Combination of selected opioids with other active substances for use in the therapy of urinary incontinence)

IT 186033-14-7, NS 8
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NS 8; opioid combination with other active substances for treatment of urinary incontinence)

IT 52-28-8, Codeine phosphate 57444-62-9, Resiniferatoxin 92725-18-3D, derivs. 93413-69-5, Venlafaxine 142155-43-9, Cizolirtine 158836-71-6, Nitro-Flurbiprofen 174636-32-9, Talnetant 175590-75-7 175590-76-8 175590-77-9 175590-78-0 175590-89-3 175590-90-6 175590-91-7 175590-92-8 175591-01-2 175591-02-3 175591-04-5 175591-05-6 175591-06-7 175591-09-0 175591-11-4 175591-12-5 175591-23-8 175591-24-9 175591-25-0 175774-12-6 175774-14-8 175774-16-0 175774-18-2 187219-61-0 187219-93-8 187219-95-0 187219-97-2 187219-99-4 187220-01-5 187220-05-9 187220-25-3 187220-29-7 217185-75-6, TAK-637 220382-87-6, Rec 15/3079 **242478-37-1**, Solifenacin 286930-03-8, Fesoterodine 433265-42-0 433265-54-4 433265-59-9 433265-65-7 433265-73-7 433686-04-5 433686-05-6 433686-06-7 433686-07-8 433936-14-2 433936-20-0 433936-23-3 433936-24-4 502616-18-4 502616-19-5 502616-20-8 502616-22-0 502616-23-1 630046-59-2 630395-07-2, SL 251039 630395-08-3, R 450 630395-09-4, DRP 001
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid combination with other active substances for treatment of urinary incontinence)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

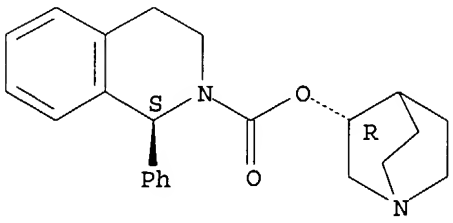
RE

(1) Durand, A; PRESSE MEDICALE 2000, V29(16), P917

(2) Gruenenthal Gmbh; DE 19947747 A 2001 HCAPLUS
(3) Kroner, B; JOURNAL OF GERIATRIC DRUG THERAPY 1992, V7(1), P23
(4) Malinovsky, J; ANESTHESIA AND ANALGESIA 1998, V87(2), P456 HCAPLUS
(5) McNutt, R; US 5658908 A 1997 HCAPLUS
(6) Novosis Pharma Ag; EP 1072260 A 2001 HCAPLUS
(7) Palmer, K; GASTROENTEROLOGY 1980, V79(6), P1272 MEDLINE
(8) Pandita, R; NEUROUROLOGY AND URODYNAMICS, 31st Annual Meeting of the International Continence Society 2001, V20(4), P439
(9) Ripple, M; AMERICAN JOURNAL OF FORENSIC MEDICINE AND PATHOLOGY 2000, V21(4), P370 MEDLINE

IT **242478-37-1**, Solifenacin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(opioid combination with other active substances for treatment of urinary incontinence)
RN 242478-37-1 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L14 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:750706 HCAPLUS
DN 139:277051
ED Entered STN: 25 Sep 2003
TI Preparation of quinuclidine derivatives as muscarine M3 receptor antagonists
IN Inakoshi, Masatoshi; Nagata, Koji; Yorimoto, Naoki; Naito, Ryo; Ikeda, Masaru; Hatanaka, Toshiki
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D453-02
ICS A61K031-439; A61K031-452; A61K031-4709; A61K031-5377; A61P001-04; A61P011-00; A61P011-02; A61P011-06; A61P013-02; A61P043-00
CC 31-5 (Alkaloids)
Section cross-reference(s): 1
FAN.CNT 1

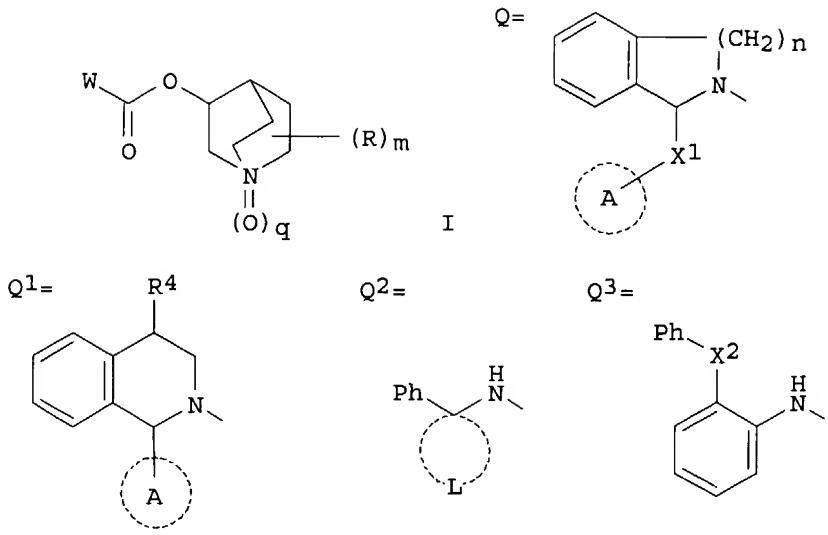
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003267977	A2	20030925	JP 2002-69621	20020314 <--
PRAI JP 2002-69621		20020314 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2003267977	ICM	C07D453-02
	ICS	A61K031-439; A61K031-452; A61K031-4709; A61K031-5377; A61P001-04; A61P011-00; A61P011-02; A61P011-06; A61P013-02; A61P043-00

OS MARPAT 139:277051

GI



AB The title compds. [I; R = halo, OR1, COR1, CO2 R1 , CON(R1)R2, S(O)pR1, NR1R2, N(R1)COR2, N(R1)CO2R2, N(R1)CON(R2)R3, N(R1)S(O)pR2, each (un)substituted lower alkyl, lower alkenyl, cycloalkyl, aryl, heteroaryl, or 5- to 6-membered ring saturated heterocyclyl; m = an integer of 1-3; q = 0, 1; wherein R1-R3 = H, each lower alkyl, lower alkenyl, cycloalkyl, aryl, heteroaryl, or 5- to 6-membered ring saturated heterocyclyl; p = 0, 1,2; W = Q-Q3, Ph2CHNH; wherein n = 1,2; the ring A = each (un)substituted aryl, cycloalkyl, heteroaryl, or 5- to 6-membered ring saturated heterocyclyl; R4 = HO, lower alkyl, lower alkoxycarbonyl; L = C2-7 alkylene optionally interrupted by O or (un)substituted NH; X1 = a single bond, CH2; X2 = a single bond, O, S], salts thereof, or N-oxides thereof or quaternary ammonium salts thereof are prepared These compds. possess muscarine M3 receptor antagonism and are useful for the treatment or prevention of urol. diseases, respiratory diseases, or digestive tract diseases. Thus, a solution of 2-ethylquinuclidin-3-ol 2.00, Et 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate 3.68, sodium ethoxide 0.18 g, 1.8 mL DMF in 37 mL toluene underwent reactive distillation at distillation rate of 3.7 mL/h
for 8 h and was extracted with 19 mL toluene and 10 mL H2O followed by extraction
of the toluene layer with 10 mL H2O and then with 5% aqueous HCl solution, adding
20 mL EtOAc and 20 mL 40% aqueous K2CO3 solution, drying the EtOAc layer over MgSO4 and evaporation under reduced pressure to give 3.6 g 2-ethylquinuclidin-3-yl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate. The compds. I exhibited high affinity to muscarine M3 receptor expressed in Chinese hamster egg-derived cells (CHO-k1).

ST quinuclidine deriv prepn muscarine M3 receptor antagonist; ethylquinuclidinyl phenyltetrahydroisoquinolinecarboxylate prepn muscarine M3 receptor antagonist; urol disease prevention treatment quinuclidine deriv prepn; respiratory disease prevention treatment quinuclidine deriv prepn; digestive tract disease prevention treatment quinuclidine deriv prepn

IT Muscarinic antagonists
(M3; preparation of quinuclidine derivs. as muscarine M3 receptor

antagonists for treatment or prevention of urol. diseases, respiratory diseases, or digestive tract diseases)

IT Muscarinic receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(M3; preparation of quinuclidine derivs. as muscarine M3 receptor antagonists for treatment or prevention of urol. diseases, respiratory diseases, or digestive tract diseases)

IT Digestive tract, disease
Respiratory tract, disease
Urinary tract, disease
(preparation of quinuclidine derivs. as muscarine M3 receptor antagonists for treatment or prevention of urol. diseases, respiratory diseases, or digestive tract diseases)

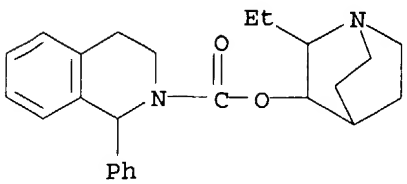
IT **605696-10-4P**, 2-Ethylquinuclidin-3-yl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate **605696-17-1P**, 2-Methylquinuclidin-3-yl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinuclidine derivs. as muscarine M3 receptor antagonists for treatment or prevention of urol. diseases, respiratory diseases, or digestive tract diseases)

IT 75-07-0, Acetaldehyde, reactions 1193-65-3, Quinuclidin-3-one hydrochloride 5291-26-9, 2-Methylenequinuclidin-3-one 180272-31-5, Ethyl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinuclidine derivs. as muscarine M3 receptor antagonists for treatment or prevention of urol. diseases, respiratory diseases, or digestive tract diseases)

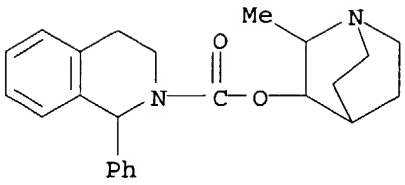
IT 5291-14-5P, 2-Methylquinuclidin-3-one 120942-87-2P, 2-Ethylquinuclidin-3-ol 155282-36-3P, 2-Ethylidenequinuclidin-3-one
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinuclidine derivs. as muscarine M3 receptor antagonists for treatment or prevention of urol. diseases, respiratory diseases, or digestive tract diseases)

IT **605696-10-4P**, 2-Ethylquinuclidin-3-yl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate **605696-17-1P**, 2-Methylquinuclidin-3-yl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinuclidine derivs. as muscarine M3 receptor antagonists for treatment or prevention of urol. diseases, respiratory diseases, or digestive tract diseases)

RN 605696-10-4 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 2-ethyl-1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 605696-17-1 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 2-methyl-1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



L14 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:723665 HCAPLUS
DN 139:235463
ED Entered STN: 16 Sep 2003
TI Intraorally disintegratable preparations for treatment of urinary disturbance and their manufacture
IN Sugimoto, Michihiko
PA Asahi Kasei Corporation, Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K009-19
ICS A61J003-06; A61K031-495; A61K047-10; A61K047-42; A61P013-02; A61P043-00
CC 63-6 (Pharmaceuticals)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003261439	A2	20030916	JP 2002-62978	20020308 <--
PRAI JP 2002-62978		20020308 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2003261439	ICM	A61K009-19
	ICS	A61J003-06; A61K031-495; A61K047-10; A61K047-42; A61P013-02; A61P043-00

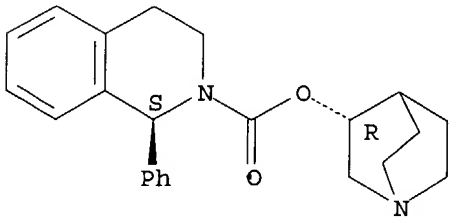
AB The prepns., useful for elderly people, are manufactured by mixing slightly soluble active ingredients with carriers, suspending in poor solvents, pouring into molds, and freeze-drying. Naftopidil powder 1, gelatin 0.14, and Mannit P 0.1 g were dispersed into H2O, poured into blister pack pockets, and freeze-dried to give tablets, which showed rapid disintegration in H2O and in mouth, no bitterness, and no unpleasant texture.
ST urinary disturbance treatment prepn oral disintegration; naftopidil oral disintegration urinary disturbance treatment
IT Micturition
(disorders; intraorally disintegratable prepns. for treatment of urinary disturbance)
IT Human
(intraorally disintegratable prepns. for treatment of urinary disturbance)
IT Drug delivery systems
(oral; intraorally disintegratable prepns. for treatment of urinary disturbance)
IT 57149-07-2, Naftopidil **242478-38-2**, YM 905
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intraorally disintegratable prepns. for treatment of urinary disturbance)
IT **242478-38-2**, YM 905
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intraorally disintegratable prepns. for treatment of urinary

disturbance)
RN 242478-38-2 HCAPLUS
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

L14 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:678653 HCAPLUS
DN 139:207821
ED Entered STN: 29 Aug 2003
TI Use of cyclooxygenase inhibitors and antimuscarinic agents for the treatment of incontinence
IN Versi, Ebrahim
PA **Pharmacia Corporation, USA**
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-12
ICS A61K031-196; A61K031-352; A61K031-5415; A61K031-135; A61P013-10
CC 1-12 (Pharmacology)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003070233	A1	20030828	WO 2003-US4561	20030214 <--

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003191172 A1 20031009 US 2003-368091 20030218 <--
PRAI US 2002-357888P P 20020219 <--
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003070233	ICM	A61K031-12
	ICS	A61K031-196; A61K031-352; A61K031-5415; A61K031-135; A61P013-10

AB The invention provides a method for the use of a cyclooxygenase-2 inhibitor, alone or in combination with an antimuscarinic agent, for the treatment or prophylaxis of a urinary incontinence condition in a subject in need of such treatment or prevention, comprising administering to the subject an effective amount of the cyclooxygenase-2 inhibitor and, optionally, the antimuscarinic agent.

ST cyclooxygenase 2 inhibitor incontinence treatment; COX2 inhibitor antimuscarinic agent incontinence treatment

IT Drug delivery systems
Muscarinic antagonists
(cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT Bladder, disease
(cystitis, interstitial; cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT Bladder, disease
(hyperreflexia; cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT Bladder, disease
(incontinence; cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT Urinary tract, disease
(infection; cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT Anti-inflammatory agents
(nonsteroidal; cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT Bladder
(overactive; cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT Drug delivery systems
(prodrugs; cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT Urethra
(suburethral diverticulitis; cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

IT 39391-18-9, Cyclooxygenase 329900-75-6, Cyclooxygenase 2
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)

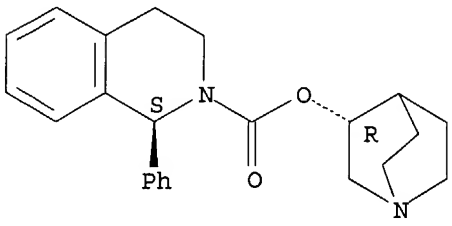
IT 50-34-0, Propantheline bromide 67-92-5, Dicyclomine hydrochloride 113-52-0, Imipramine hydrochloride 254-04-6D, Benzopyran, derivs. 590-63-6, Bethanechol chloride 620-61-1, Hyoscyamine sulfate 1508-65-2, Oxybutynin chloride 7082-21-5, Terodiline chloride 10405-02-4, Trospium chloride 29828-28-2D, Dihydronaphthalene, derivs. 29968-14-7D, Dihydroquinoline, derivs. 54556-98-8, Propiverine hydrochloride 71125-38-7, Meloxicam 123653-11-2, NS-398 124937-52-6, Tolterodine tartrate 129927-33-9, Temiverine hydrochloride 138555-49-4 138951-54-9, FK-584 162011-90-7, Rofecoxib 169590-41-4, Deracoxib 169590-42-5, Celecoxib 170105-16-5, KRP-197 171722-81-9, YM-46303 179382-91-3, RS-57067 180200-68-4, JTE-522 181695-72-7, Valdecoxib 198470-84-7, Parecoxib 202409-33-4, Etoricoxib 220991-20-8, COX-189 230949-16-3 **242478-38-2**, YM-905 266320-83-6, ABT-963 337359-08-7, AH-9700 586346-93-2 586346-94-3 586346-95-4 586346-96-5 586957-44-0, Zamifenacin hydrochloride 587021-49-6, J

104135
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Appell, R; UROLOGY 1997, V50(6A SUPPL), P90 MEDLINE
(2) Cardozo, L; BRITISH MEDICAL JOURNAL 1980, V280(6210), P281 MEDLINE
(3) Cardozo, L; THE JOURNAL OF UROLOGY 1980, V123(3), P399 MEDLINE
(4) Layton, D; DRUG SAFETY 2001, V24(9), P703 HCAPLUS
(5) Lecci, A; BRITISH JOURNAL OF PHARMACOLOGY 2000, V130(2), P331 HCAPLUS
(6) Merck Frosst Canada Inc; WO 0215902 A 2002 HCAPLUS
(7) Nicox Sa; WO 9809948 A 1998 HCAPLUS
(8) Nilvebrant, L; EUROPEAN JOURNAL OF PHARMACOLOGY 1997, V327, P195 HCAPLUS
(9) Recordati Chem Pharm; WO 02080927 A 2002
(10) Theoharides, T; EXPERT OPINION ON INVESTIGATIONAL DRUGS 2001, V10(3), P521 HCAPLUS
IT **242478-38-2**, YM-905
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase inhibitors and antimuscarinic agents for treatment of incontinence)
RN 242478-38-2 HCAPLUS
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

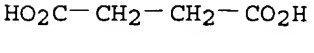
CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4



L14 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:652131 HCAPLUS
DN 139:214237
ED Entered STN: 21 Aug 2003
TI Preparation of nitrate prodrugs able to release nitric oxide in a controlled and selective way and their use for prevention and treatment of inflammatory, ischemic and proliferative diseases

IN Scaramuzzino, Giovanni
PA Italy
SO Eur. Pat. Appl., 313 pp.
CODEN: EPXXDW
DT Patent
LA English
IC ICM C07C205-00
ICS A61K031-00
CC 26-1 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1, 28, 29, 33, 34, 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 1336602	A1	20030820	EP 2002-425075	20020213 <--

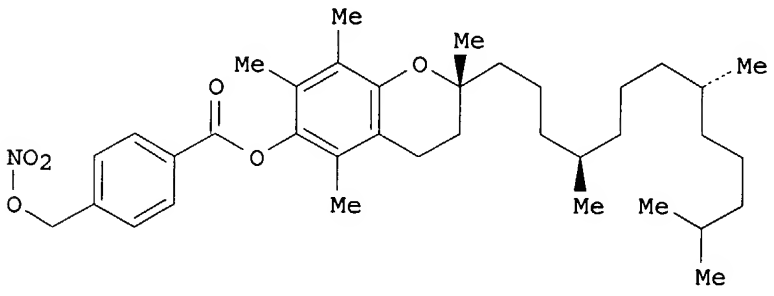
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI EP 2002-425075 20020213 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 1336602	ICM	C07C205-00
	ICS	A61K031-00

GI



II

AB New pharmaceutical compds. of general formula F-(X)q (I) [q = 1-5, preferably 1; F is chosen among drugs such as δ-tocopherol, clidanac, diethylhomospermine, glucosamine, thymocartin, vofopitant, etc.; X is chosen among 4 groups M, T, V, and Y where M = ONO2, nitrate salt, nitrite ester, ONO, thoinitrite, SNO, etc., T = OR1-M, OR1OR1-M, SR1NR2R1-M, NR2R1-M, NR2R1SR1-M, etc., R1 = saturated or unsatd., linear or branched alkylene, having 1 to 21 carbon atoms or a saturated or unsatd., optionally heterosubstituted or branched cycloalkylene, having 3 to 7 carbon atoms or an optionally heterosubstituted arylene having 3 to 7 carbon atoms; R2 = H, saturated or unsatd., linear or branched 1-21 carbon atom alkyl, saturated or unsatd. optionally heterosubstituted or branched 3-7 carbon cycloalkyl, optionally heterosubstituted 3-7 carbon aryl; R1, R2 = OH, SH, F, Cl, Br, OPO3H2, CO2H, etc.; bond between F and T = carboxylic ester, carboxylic amide, glycoside, azo, thioester, sulfonic ester, etc.; V = Z-M2, OZ-M2, NR2Z-M2, R1Z-M2, OR1-M2, OR1Z-M2, M2 = M, R1-M, OR1-M, SR1-M, NR2R1-M; ZM2 = COCH2CH(M2)CH2N+Me3, COCH2CH2COM2, COCH(NHR2)CH2M2, etc.; Y = 4-COC6H4CH2ONO2, O(CH2)4ONO2, COCH(NH2)CH2ONO2, 3-OC6H4CH2ONO2, etc.] were prepared For example, α-tocopherol reacted with 4-HO2CC6H4CH2ONO2 to give the nitroxymethyl derivative II. The compds. of general formula I are nitrate prodrugs which can release nitric oxide in vivo in a controlled and selective way and without hypotensive side effects and for this reason they are useful for the preparation of medicines for prevention and treatment of inflammatory, ischemic, degenerative and proliferative diseases of musculoskeletal, tegumental, respiratory, gastrointestinal, genito-urinary and central nervous systems.

ST nitrate prodrug prepn; inflammation nitrate prodrug; ischemia nitrate prodrug; proliferative disease nitrate prodrug; degenerative disease nitrate prodrug; musculoskeletal disease nitrate prodrug; respiratory disease nitrate prodrug; gastrointestinal disease nitrate prodrug; genito urinary disease nitrate prodrug; central nervous system disease nitrate prodrug; tegumental disease nitrate prodrug

IT Intestine, disease
(Crohn's; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Bone, disease
(Paget's; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Respiratory distress syndrome
(adult; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Prostate gland, disease
(benign hyperplasia; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Bronchi, disease
(bronchitis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Nervous system, disease
(central; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Lung, disease
(chronic obstructive; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Intestine, neoplasm
(colorectal; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Disease, animal
(degenerative; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Sexual behavior
(disorder; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Intestine, disease
(duodenum, ulcer; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Invertebrate body covering
(epidermis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Esophagus, disease
(esophagitis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Intestine, neoplasm
(familial polyposis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Stomach, disease
(gastritis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Bladder, disease
(incontinence; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Muscle
(musculoskeletal diseases; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Hemoglobins
RL: BSU (Biological study, unclassified); BIOL (Biological study)

(nitrosylHbs; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Pancreas, disease
(pancreatitis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Allergy
Alzheimer's disease
Anti-inflammatory agents
Anti-ischemic agents
Antitumor agents
Asthma
Bladder, neoplasm
Blood pressure
Brain, neoplasm
Cirrhosis
Cystic fibrosis
Dermatitis
Digestive tract, disease
Emphysema
Esophagus, neoplasm
Inflammation
Ischemia
Liver, neoplasm
Lung, neoplasm
Mammary gland, neoplasm
Multiple sclerosis
Osteoarthritis
Osteoporosis
Ovary, neoplasm
Pancreas, neoplasm
Prostate gland, neoplasm
Psoriasis
Reproductive tract, disease
Respiratory tract, disease
Rheumatoid arthritis
Skin, neoplasm
Stomach, neoplasm
Ulcer
Urinary tract, disease
Uterus, neoplasm
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Drug delivery systems
(prodrugs; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Disease, animal
(proliferative; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Prostate gland, disease
(prostatitis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Nose, disease
(rhinitis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Lupus erythematosus
(systemic; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Digestive tract, disease
(ulcer, peptic; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT Intestine, disease
(ulcerative colitis; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative

diseases)

IT Biological transport
(uptake; preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT 55-63-0, Nitroglycerine 78-11-5, Pentaerythritol tetranitrate 87-33-2, Isosorbide dinitrate 14402-89-2, Sodium nitroprusside 16051-77-7, Isosorbide mononitrate 65141-46-0, Nicorandil 206197-03-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT 586347-22-0P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT 327610-87-7P 571186-50-0P 571186-51-1P 586347-27-5P 586347-30-0P 586347-40-2P 586347-41-3P 586347-44-6P
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT 50-23-7, Hydrocortisone
RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT 586347-24-2P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT 13005-09-9P 96513-33-6P 116539-59-4P 198483-54-4P 257625-98-2P
329976-33-2P 352464-98-3P 398454-56-3P 398460-42-9P 410071-16-8P
571186-52-2P 586347-21-9P 586347-23-1P 586347-25-3P 586347-26-4P
586347-28-6P 586347-29-7P 586347-31-1P 586347-32-2P 586347-33-3P
586347-34-4P 586347-36-6P 586347-38-8P 586347-39-9P 586347-42-4P
586347-43-5P 586347-45-7P 586347-46-8P 586347-47-9P 586347-48-0P
586347-50-4P 586347-51-5P 586347-52-6P 586347-53-7P 586347-54-8P
586347-55-9P 586347-56-0P 586347-57-1P 586347-58-2P 586347-60-6P
586347-62-8P 586347-63-9P 586347-64-0P 586347-65-1P 586347-66-2P
586347-68-4P 586347-69-5P 586347-70-8P 586347-72-0P 586347-73-1P
586347-75-3P 586347-76-4P 586347-77-5P 586347-79-7P 586347-80-0P
586347-81-1P 586347-82-2P 586347-86-6P 586347-92-4P 586347-94-6P
586347-95-7P 586347-97-9P 586348-00-7P 586348-01-8P 586348-03-0P
586348-04-1P 586348-05-2P 586348-07-4P 586348-08-5P 586348-09-6P
586348-10-9P 586348-11-0P 586348-12-1P 586348-13-2P 586348-14-3P
586348-15-4P 586348-16-5P 586348-17-6P 586348-18-7P 586348-19-8P
586348-20-1P 586348-22-3P 586348-23-4P 586348-24-5P 586348-25-6P
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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

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RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT 50-02-2, Dexamethasone 50-24-8, Prednisolone 53-43-0, Prasterone
59-02-9, α-Tocopherol 66-84-2, D-Glucosamine hydrochloride
69-72-7, Salicylic acid, reactions 73-05-2, Phentolamine hydrochloride
83-88-5, Riboflavin, reactions 103-90-2, Acetaminophen 108-88-3,
Toluene, reactions 117-39-5, Quercetin 128-13-2, Ursodiol 132-69-4,
Benzydamine hydrochloride 620-24-6, 3-Hydroxybenzyl alcohol 876-08-4,
4-(Chloromethyl)benzoyl chloride 927-58-2, 4-Bromobutyryl chloride
2170-03-8, Itaconic anhydride 6232-88-8, 4-(Bromomethyl)benzoic acid
33036-62-3, 4-Bromobutan-1-ol 51333-22-3, Budesonide 56296-78-7,
Fluoxetine hydrochloride 80573-04-2, Balsalazide 82413-20-5,
Droloxifene 92340-57-3, 5-Hydroxyomeprazole 119169-78-7, Epristeride

131926-98-2, 5-Hydroxylansoprazole 136434-34-9, Duloxetine hydrochloride
151602-49-2, 5-O-Desmethylomeprazole 169590-42-5, Celecoxib
181695-72-7, Valdecoxib
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

IT 19340-33-1P 101014-64-6P 101973-77-7P 116081-53-9P 116973-12-7P
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586347-37-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Astrazeneca Ab; WO 0072838 A 2000 HCAPLUS
(2) Benedi; WO 0230866 A 2002 HCAPLUS
(3) Cirino; BRIT J PHARMACOL 1996, V117, P1421 HCAPLUS
(4) Currie, M; US 5985862 A 1999 HCAPLUS
(5) Endres, S; EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY 1999, V11(34), P895
(6) Kawashima; CHEM PHARM BULL 1993, V41(6), P1060 HCAPLUS
(7) Kawashima; J MED CHEM 1993, V36, P815 HCAPLUS
(8) Keeble; BRIT J PHARMACOL 2001, V133, P1023 HCAPLUS
(9) Lehmann; ARCH PHARM PHARM MED CHEM 1997, V330(8), P247 HCAPLUS
(10) Lundy; US 2001012851 A1 2001
(11) Nicox Sa; WO 0230867 A 2002 HCAPLUS
(12) Ogawa; CHEM PHARM BULL 1993, V41(6), P1049 HCAPLUS
(13) Pfizer Prod Inc; EP 0984012 A 2000 HCAPLUS
(14) Searle & Co; WO 9721721 A 1997 HCAPLUS
(15) Searle & Co; WO 9721724 A 1997 HCAPLUS
(16) Searle & Co; WO 9740836 A 1997 HCAPLUS
(17) Tallet, D; BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS 2002, V290(1), P125 HCAPLUS
(18) Tashima, K; LIFE SCIENCES 2000, V67(13), P1639 HCAPLUS
(19) Yissum Res Dev Co; WO 9842661 A 1998 HCAPLUS

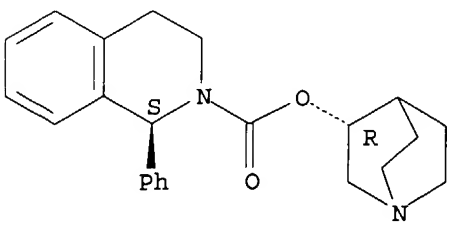
IT **586349-90-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of nitrate prodrugs for treating or preventing inflammatory, ischemic, degenerative, and proliferative diseases)

RN 586349-90-8 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)-, mononitrate (9CI) (CA INDEX NAME)

CM 1

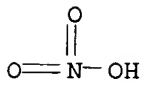
CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 7697-37-2
CMF H N O3



L14 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:57905 HCAPLUS
DN 138:100946
ED Entered STN: 24 Jan 2003
TI Medicinal composition for treatment of interstitial cystitis
IN Ikeda, Ken; Takeuchi, Makoto
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM A61K031-439
ICS A61P013-02; A61P013-10; A61P025-02; C07D453-02
CC 1-11 (Pharmacology)
Section cross-reference(s): 63
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003006019	A1	20030123	WO 2002-JP6904	20020708 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
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BR 2002010873	A	20040622	BR 2002-10873	20020708 <--
US 2004138252	A1	20040715	US 2003-479798	20031205 <--
PRAI JP 2001-209041	A	20010710 <--		
WO 2002-JP6904	W	20020708 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2003006019	ICM	A61K031-439
	ICS	A61P013-02; A61P013-10; A61P025-02; C07D453-02

AB A capsaicin-sensitive sensory nerve depressant which contains quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate or a salt thereof as the active ingredient. It is a remedy for a urol. disease selected among interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis.
ST quinuclidineylphenyltetrahydroisoquinolinecarboxylate bladder interstitial cystitis prostatitis
IT Drug delivery systems
(capsules; quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-

carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

IT Bladder, disease
(interstitial cystitis; quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

IT Urinary tract
(lower, hyperesthesia; quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

IT Drug delivery systems
(oral; quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

IT Prostate gland, disease
(prostatitis; quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

IT Nerve
(sensory, urinary bladder; quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

IT 404-86-4, Capsaicin
RL: PAC (Pharmacological activity); BIOL (Biological study)
(quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

IT **180272-14-4 180272-14-4D**, salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD

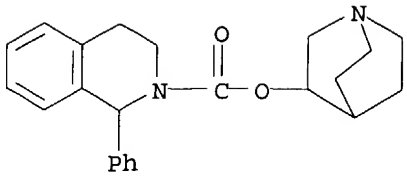
RE

(1) Yamanouchi Pharmaceutical Co Ltd; CN 1171109 A 1996 HCAPLUS
(2) Yamanouchi Pharmaceutical Co Ltd; CA 2208839 A 1996 HCAPLUS
(3) Yamanouchi Pharmaceutical Co Ltd; NZ 298144 A 1996
(4) Yamanouchi Pharmaceutical Co Ltd; PL 321019 A 1996
(5) Yamanouchi Pharmaceutical Co Ltd; AU 4355396 A 1996
(6) Yamanouchi Pharmaceutical Co Ltd; US 6017927 A 1996 HCAPLUS
(7) Yamanouchi Pharmaceutical Co Ltd; HU 77006 A 1996 HCAPLUS
(8) Yamanouchi Pharmaceutical Co Ltd; EP 801067 A1 1996 HCAPLUS
(9) Yamanouchi Pharmaceutical Co Ltd; WO 9620194 A1 1996 HCAPLUS
(10) Yamanouchi Pharmaceutical Co Ltd; FI 972775 A 1996
(11) Yamanouchi Pharmaceutical Co Ltd; NO 973027 A 1996

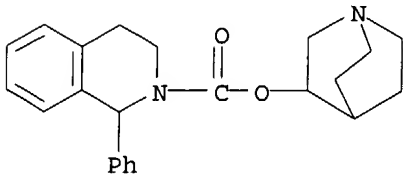
IT **180272-14-4 180272-14-4D**, salts
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinuclidine-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate and its salts for treatment of interstitial cystitis, hyperesthesia in the lower urinary tract, and prostatitis)

RN 180272-14-4 HCAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-14-4 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



L14 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:554144 HCAPLUS
DN 137:163148
ED Entered STN: 26 Jul 2002
TI Irritable bowel syndrome neuropharmacology: A review of approved and investigational compounds
AU Callahan, Michael J.
CS Department of Medical Affairs, Novartis Pharmaceuticals Inc., East Hanover, NJ, 07936, USA
SO Journal of Clinical Gastroenterology (**2002**), 35(1, Suppl.), S58-S67
CODEN: JCGADC; ISSN: 0192-0790
PB Lippincott Williams & Wilkins
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review. Anticholinergics and prokinetics are mainstays of therapy for Irritable Bowel Syndrome (IBS) patients despite their limited efficacy and troublesome side-effect profile. The clin. limitations of these drugs are a result of their relative broad and nonspecific pharmacol. interaction with various receptors. Recent advances in gut physiol. have led to the identification of various receptor targets that may play a pivotal role in the pathogenesis of IBS. Medicinal chemists searching for safe and effective IBS therapies are now developing compds. targeting many of these specific receptors. The latest generation of anticholinergics, such as zamifenacin, darifenacin, and YM-905, provide selective antagonism of the muscarinic type-3 receptor. Tegaserod, a selective 5-HT4 partial agonist, tested in multiple clin. trials, is effective in reducing the symptoms of abdominal pain, bloating, and constipation. Ezlopitant and nepadudant, selective antagonists for neurokinin receptors type 1 and type 2, resp., show promise in reducing gut motility and pain. Loperamide, a mu (μ) opioid receptor agonist, is safe and effective for IBS patients with diarrhea (IBS-D) as the predominant bowel syndrome. Fedotozine, a kappa (κ) opioid receptor agonist, has been tried as a visceral analgesic in various clin. trials with conflicting results. Alosetron, a 5-HT3 receptor antagonist, has demonstrated efficacy in IBS-D patients but incidents of ischemic colitis seen in post-marketing follow-up resulted its removal from the market. Compds. that target cholecystokinin A, N-methyl-D-aspartate, alpha2-adrenergic, and corticotropin-releasing factor receptors are also examined in this review.

ST review drug receptor irritable bowel syndrome
IT Human
(irritable bowel syndrome neuropharmacol.: review of approved and investigational compds.)
IT Receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(irritable bowel syndrome neuropharmacol.: review of approved and investigational compds.)
IT Intestine, disease
(irritable bowel syndrome; irritable bowel syndrome neuropharmacol.: review of approved and investigational compds.)
IT 183747-35-5, Nepadutant
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MEN-11420; irritable bowel syndrome neuropharmacol.: review of approved and investigational compds.)
IT 53179-11-6, Loperamide 122852-42-0, Alosetron 123618-00-8, Fedotozine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(irritable bowel syndrome neuropharmacol.: review of approved and investigational compds.)
IT 127308-82-1, Zamifenacin 133099-04-4, Darifenacin 145158-71-0, Tegaserod 147116-64-1, Ezlopitant **242478-38-2**, YM-905
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irritable bowel syndrome neuropharmacol.: review of approved and investigational compds.)
RE.CNT 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) American College of Gastroenterology Committee on FDA Related matters; Am J Gastroenterol 1983, V78, P189
(2) Anon; Gastrointestinal pharmacology 1993
(3) Anon; www.micromedex.com 2001
(4) Anonymous; Practitioner 1976, V217, P276
(5) Anton, P; Pain 2001, V92, P219 HCAPLUS
(6) Awad, R; Acta Gastroenterol Latinoam 2000, V30, P169 MEDLINE
(7) Awouters, F; Annu Rev Pharmacol Toxicol 1983, V23, P279 HCAPLUS
(8) Bouras, E; Gastroenterology 2001, V210, P354
(9) Bouras, E; Gut 1999, V44, P682 HCAPLUS
(10) Briejer, M; Gastroenterology 1997, V112, PA705
(11) Briejer, M; Gastroenterology 1997, V112, PA705
(12) Buchheit, K; J Med Chem 1995, V38, P2326 HCAPLUS
(13) Camilleri, M; Aliment Pharmacol Ther 2001, V15, P277 HCAPLUS
(14) Camilleri, M; Arch Intern Med 2001, V161, P1733 HCAPLUS
(15) Cammilleri, M; Gastroenterology 2001, V120, P652
(16) Cann, P; Dig Dis Sci 1984, V29, P239 MEDLINE
(17) Cann, P; Gut 1983, V24, P1135 MEDLINE
(18) Catalioto, R; Br J Pharmacol 1998, V123, P81 HCAPLUS
(19) Chey, W; Am J Gastroenterol 2001, V96, P1499 MEDLINE
(20) Chochrane, S; Gastroenterology 2001, V120, PA7
(21) Christinaki, H; 13th International Symposium on Medicinal Chemistry 1994, PP144
(22) Coulie, B; Gastroenterology 1997, V112, PA715
(23) Coulie, B; Gastroenterology 1997, V112, PA715
(24) Coupar, I; Life Sci 1987, V41, P917 HCAPLUS
(25) Coutinho, S; Brain Res 1996, V736, P7 HCAPLUS
(26) Dapoigny, M; Dig Dis Sci 1995, V40, P2244 HCAPLUS
(27) DePonti, F; Pharmacol Ther 1998, V89, P49
(28) DeSchryver, A; Scand J Gastroenterol 2000, V34(Suppl 232), P38
(29) De Tullio, P; Exp Opin Invest Drugs 2000, V9, P129 HCAPLUS
(30) Degen, L; Aliment Pharmacol Ther 2001, V15, P1745 HCAPLUS
(31) Delvaux, M; Expert Opin Investig Drugs 2001, V10, P97 HCAPLUS
(32) Dunphy, C; Drugs Aging 2001, V18, P201
(33) Edwards, C; Gut 1987, V28, P13 HCAPLUS
(34) Eglen, R; Life Sci 2001, V68, P2573 HCAPLUS
(35) Emmanuel, A; Gut 1998, V42, P511 HCAPLUS

(36) Farup, P; Scand J Gastroenterol 1998, V33, P128 HCAPLUS
(37) Fielding, J; Digestion 1982, V23, P125 MEDLINE
(38) Gates, T; Peptides 1988, V9, P1207 HCAPLUS
(39) Gershon, M; Aliment Pharmacol Ther 1999, V13(Suppl 2), P15
(40) Goldberg, P; Digestion 1996, V57, P478 HCAPLUS
(41) Goyal, R; N Engl J Med 1996, V334, P1106 MEDLINE
(42) Grider, J; Am J Physiol 1989, V257, PG709 HCAPLUS
(43) Hardcastle, J; J Pharm Pharmacol 1998, V50, P539 HCAPLUS
(44) Hargreaves, A; Mol Pharmacol 1994, V46, P1120 HCAPLUS
(45) Holzer, P; Pharmacol Ther 1997, V73, P173 HCAPLUS
(46) Houghton, L; Aliment Pharmacol Ther 1999, V13, P1437 HCAPLUS
(47) Hovdenak, N; Scand J Gastroenterol 1987, V130, P81 MEDLINE
(48) Jailwala, J; Ann Intern Med 2000, V133, P136 HCAPLUS
(49) Kahrilas, P; Aliment Pharmacol Ther 2000, V14, P1503 HCAPLUS
(50) Kajita, S; Pharmacology 2001, V63, P8 HCAPLUS
(51) Kishimoto, S; Regul Pept 1991, V36, P65
(52) Klien, K; Gastroenterology 1988, V95, P232
(53) Kobayashi, S; Jpn J Pharmacol 2001, V86, P281 HCAPLUS
(54) Krevksy, B; Aliment Pharmacol Ther 1987, V1, P293
(55) Lefkowitz, M; Digestion 1998, V9(Suppl 3), P735
(56) Lembo, T; Am J Gastroenterol 2001, V96, P2662 HCAPLUS
(57) Liddle, R; Ann Rev Physiol 1997, V59, P221 HCAPLUS
(58) Lordal, M; Br J Pharmacol 2001, V134, P215 HCAPLUS
(59) Lotstra, F; Peptides 1987, V8, P911 HCAPLUS
(60) Maggi, C; Naunyn Schmiedeberg's Arch Pharmacol 1990, V341, P256 HCAPLUS
(61) Matts, S; Br J Clin Pract 1967, V21, P549 MEDLINE
(62) McRoberts, J; Gastroenterology 2001, V120, P1737 HCAPLUS
(63) Meyer, B; Lancet 1989, V2, P12 MEDLINE
(64) Milo, R; Curr Med Res Opin 1980, V6, P577 MEDLINE
(65) Mine, Y; J Pharmacol Exp Ther 1997, V283, P1000 HCAPLUS
(66) Moran, T; Brain Res 1986, V362, P175 HCAPLUS
(67) Moran, T; Regul Pept Lett 1994, V6, P6
(68) Moriarty, D; Am J Physio Cell Physiol 2001, V49, PC852
(69) Morini, G; Regul Pept 1990, V20, P313
(70) Moss, H; Br J Pharmacol 1990, V100, P497 HCAPLUS
(71) Muller-Lissner, S; Aliment Pharmacol Ther 2001, V15, P1655 HCAPLUS
(72) Nagakura, Y; Pharmacol Res 1999, V39, P375 HCAPLUS
(73) Nigan, P; J Assoc Physicians India 1984, V32, P1041
(74) Ogishima, M; J Pharmacol Exp Ther 2000, V294, P33 HCAPLUS
(75) Oh-Young, L; Gastroenterology 2000, V118, PA846
(76) Pace, F; Digestion 1995, V56, P433 MEDLINE
(77) Page, J; J Clin Gastroenterol 1981, V3, P153 MEDLINE
(78) Patacchini, R; Eur J Pharmacol 2001, V398, P389
(79) Prior, A; Aliment Phramacol Ther 1993, V7, P175 MEDLINE
(80) Rawls, J; Gut 2000, V47, PA217
(81) Sandier, R; Gastroenterology 1990, V99, P409
(82) Schikowski, A; Gastroenterology 1999, V117, PA643
(83) Schutze, K; Aliment Pharmacol Ther 1997, V11, P387 HCAPLUS
(84) Schuurkes, J; Scand J Gastroenterol 1984, V96(Suppl), P101
(85) Shulkes, A; Clin Exp Pharmacol Physiol 1997, V24, P209 MEDLINE
(86) Soll, A; Am J Physiol 1985, V248, PG569 MEDLINE
(87) Song, C; J Pharmacol Exp Ther 1997, V281, P1312 HCAPLUS
(88) Stoner, M; Gastroenterology 1998, V116, PA648
(89) Szarka, L; Gastroenterology 1999, V116, PA1089
(90) Talley, N; Lancet 2001, V358, P2061 MEDLINE
(91) Thumshirn, M; Gastroenterology 1999, V116, P573 HCAPLUS
(92) Tonini, M; Gastroenterology 2001, V120, P938 HCAPLUS
(93) Unnerstall, J; Brain Res 1984, V319, P69 MEDLINE
(94) Van Outryve, M; J Clin Gastroenterol 1991, V13, P49 MEDLINE
(95) Viramontes, B; Gastroenterology 2000, V118, PA848
(96) Wallis, R; Life Sci 1995, V56, P861 HCAPLUS
(97) Wattchow, D; Gastroenterology 1987, V93, P1363 MEDLINE
(98) Wattchow, D; Gastroenterology 1988, V95, P32 HCAPLUS

(99) Whorwell, P; Gastroenterology 2000, V118, PA1204
(100) Wood, J; Functional disorders of the gut 1998, P19

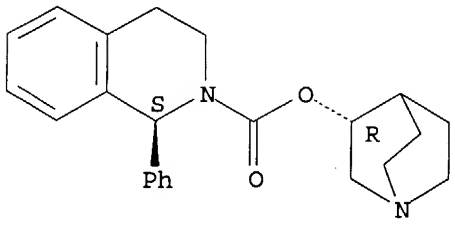
IT **242478-38-2**, YM-905
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(irritable bowel syndrome neuropharmacol.: review of approved and investigational compds.)

RN 242478-38-2 HCAPLUS
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

L14 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:525396 HCAPLUS
DN 138:198423
ED Entered STN: 15 Jul 2002
TI M3 receptor antagonism by the novel antimuscarinic agent solifenacin in the urinary bladder and salivary gland
AU Ikeda, Ken; Kobayashi, Seiji; Suzuki, Mami; Miyata, Keiji; Takeuchi, Makoto; Yamada, Toshimitsu; Honda, Kazuo
CS Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co. Ltd., 21 Miyukigaoka, Tsukuba, Ibaraki, 3058585, Japan
SO Naunyn-Schmiedeberg's Archives of Pharmacology (**2002**), 366(2), 97-103
CODEN: NSAPCC; ISSN: 0028-1298
PB Springer-Verlag
DT Journal
LA English
CC 1-11 (Pharmacology)
AB The antimuscarinic profile of the exptl. drug solifenacin/YM905 [(+)-(1S,3'R)-quinuclidin-3'-yl-1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate] for the treatment of overactive bladder was compared with the commonly prescribed agent oxybutynin. In radioligand binding assays, pKi values of solifenacin for M1, M2, and M3 receptors were 7.6, 6.9, and 8.0, resp. These values for oxybutynin were 8.6 (M1), 7.7 (M2), and 8.9 (M3). Solifenacin and oxybutynin antagonized the contractile effect of carbachol

(CCh) on isolated guinea pig urinary bladder smooth muscle (detrusor), displaying the neg. logarithm of antagonist apparent affinity constant (pKb value) of 7.1 for solifenacin and 7.4 for oxybutynin. To study the tissue selectivity between bladders and salivary glands, guinea pig detrusor and mouse submandibular gland cells were stimulated with CCh and monitored for intracellular Ca2+, as determined by Fura 2 fluorescence. Ca2+ mobilization of detrusor cells was inhibited equipotently by solifenacin (pKi=8.4) and oxybutynin (pKi=8.6), whereas that of the gland cells was antagonized less potently by solifenacin (pKb=7.4) than by oxybutynin (pKb=8.8), although the M3 subtype mediated both cell responses. In anesthetized rats, solifenacin (63-2100 nmol kg-1 or 0.03-1 mg kg-1) dose-dependently inhibited CCh-stimulated increases in urinary bladder pressure, while its inhibitory effects on salivation and bradycardia were apparent only at a dose of 2100 nmol kg-1. In contrast, oxybutynin within a dose range of 77-770 nmol kg-1 (0.03-0.3 mg kg-1) inhibited responses of the bladder and salivary gland slightly more potently than that of the heart. In addition, inhibitory effects of darifenacin indicated a major role of M3 receptors in the bladder and salivary gland. Therefore, M3 receptor antagonism by solifenacin could be bladder-selective. This selectivity remains to be elucidated and may provide new approaches to the pharmacotherapy of overactive bladder.

ST overactive bladder M3 antagonist solifenacin

IT Bladder
Salivary gland
(M3 receptor antagonism solifenacin in urinary bladder and salivary gland)

IT Muscarinic antagonists
(M3; M3 receptor antagonism solifenacin in urinary bladder and salivary gland)

IT Heart, disease
(bradycardia; M3 receptor antagonism solifenacin in urinary bladder and salivary gland)

IT Bladder
(detrusor muscle; M3 receptor antagonism solifenacin in urinary bladder and salivary gland)

IT 5633-20-5, Oxybutynin
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(M3 receptor antagonism solifenacin in urinary bladder and salivary gland)

IT **242478-37-1**, Solifenacin **242478-38-2**, YM905
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(M3 receptor antagonism solifenacin in urinary bladder and salivary gland)

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

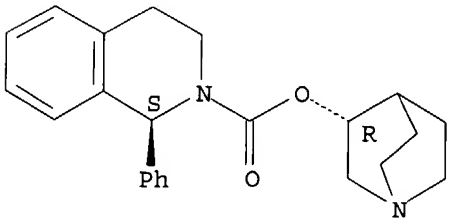
(1) Andersson, K; Baillieres Best Pract Res Clin Obstet Gynaecol 2000, V14, P291 MEDLINE
(2) Caulfield, M; Pharmacol Rev 1998, V50, P279 HCAPLUS
(3) Chapple, C; Urology 2000, V55(5A), P33
(4) Eglen, R; Curr Opin Chem Biol 1999, V3, P426 HCAPLUS
(5) Eglen, R; Pharmacol Rev 1996, V48, P531 HCAPLUS
(6) Gillberg, P; Eur J Pharmacol 1998, V349, P285 HCAPLUS
(7) Grynkiewicz, G; J Biol Chem 1985, V260, P3440 HCAPLUS
(8) Hegde, S; Br J Pharmacol 1997, V120, P1409 HCAPLUS
(9) Igawa, Y; Urology 2000, V55(5A), P47
(10) Ikeda, K; Life Sci 1999, V65, P1569 HCAPLUS
(11) Ishikawa, Y; Biochem Biophys Res Commun 1998, V245, P835 HCAPLUS
(12) Kachur, J; J Pharmacol Exp Ther 1988, V247, P867 HCAPLUS
(13) Kaiser, C; J Med Chem 1993, V36, P610 HCAPLUS
(14) Kenakin, T; Trends Pharmacol Sci 1982, V3, P153 HCAPLUS
(15) Lazareno, S; Br J Pharmacol 1993, V109, P1110 HCAPLUS

(16) Matsui, M; Proc Natl Acad Sci USA 2000, V97, P9579 HCAPLUS
(17) Melvin, J; Am J Physiol 1991, V261, PG1043 HCAPLUS
(18) Naito, R; Chem Pharm Bull 1998, V46, P1274 HCAPLUS
(19) Nilvebrant, L; Eur J Pharmacol 1997, V327, P195 HCAPLUS
(20) Noronha-Blob, L; Eur J Pharmacol 1991, V201, P135 HCAPLUS
(21) Poch, G; Br J Pharmacol 1992, V106, P710 MEDLINE
(22) Sato, K; Am J Physiol 1994, V267, PC1666 HCAPLUS
(23) Stengel, P; J Pharmacol Exp Ther 2000, V292, P877 HCAPLUS
(24) Wada, Y; Arch Int Pharmacodyn Ther 1995, V330, P76 HCAPLUS
(25) Wang, P; J Pharmacol Exp Ther 1995, V273, P959 HCAPLUS

IT **242478-37-1**, Solifenacin **242478-38-2**, YM905
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(M3 receptor antagonism solifenacin in urinary bladder and salivary gland)

RN 242478-37-1 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

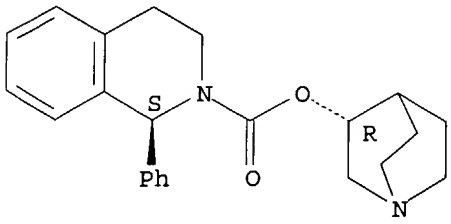


RN 242478-38-2 HCAPLUS
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

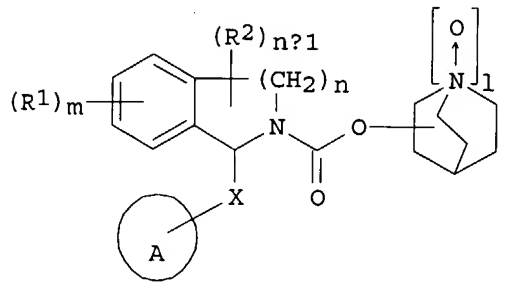
L14 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:268535 HCAPLUS
DN 136:299715
ED Entered STN: 10 Apr 2002
TI Quinuclidine derivatives as ciliary muscle relaxants
IN Kawamoto, Yoko; Waki, Mitsunori
PA Senju Pharmaceutical Co., Ltd., Japan; Yamanouchi Pharmaceutical Co., Ltd.
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM A61K031-4725
ICS A61P021-02; A61P027-02; C07D453-02
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002104968	A2	20020410	JP 2000-296464	20000928 <--
PRAI JP 2000-296464		20000928 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 2002104968	ICM	A61K031-4725
	ICS	A61P021-02; A61P027-02; C07D453-02

OS MARPAT 136:299715
GI



I

AB The invention provides a quinuclidine derivative I (A = cyclic aryl, cycloalkyl, cycloalkenyl, etc; X = single bond, methylene; R1 = halogen, OH, lower alkoxy, carboxyl, lower alkoxycarbonyl, lower acyl, mercapto, etc.; R2 = H, OH, lower alkoxy, lower alkyl; l = 0-1; m = 0-3; n = 1-2) or its salt or ternary ammonium compound, suitable for use as a ciliary muscle relaxant for prevention or treatment of myopia, asthenopia, and glaucoma. An eyedrop containing (1S,3'R)-3'-quinuclidinyl-1-phenyl-1,2,3,4-tetrahydro-2-isoquinoline carboxylate succinate 3, sodium monohydrogen phosphate dodecahydrate 0.1, NaCl 0.9, HCl q.s. to pH = 7, benzalkonium chloride 0.005 g, and water balance to 100 mL was formulated, and tested its effect on carbachol-induced contraction of ciliary muscle in rabbit eyes.
ST quinuclidine deriv ciliary muscle relaxant
IT Eye, disease
(asthenopia, treatment of; quinuclidine derivs. as ciliary muscle relaxants)
IT Eye
(ciliary muscle; quinuclidine derivs. as ciliary muscle relaxants)
IT Muscle
(ciliary; quinuclidine derivs. as ciliary muscle relaxants)
IT Vision

(myopia, treatment of; quinuclidine derivs. as ciliary muscle relaxants)

IT Antiglaucoma agents
Muscle relaxants
(quinuclidine derivs. as ciliary muscle relaxants)

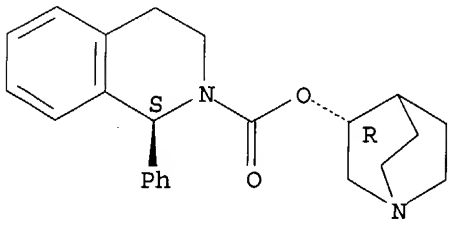
IT Drug delivery systems
(solns., ophthalmic; quinuclidine derivs. as ciliary muscle relaxants)

IT **242478-37-1 242478-38-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinuclidine derivs. as ciliary muscle relaxants)

IT **242478-37-1 242478-38-2**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quinuclidine derivs. as ciliary muscle relaxants)

RN 242478-37-1 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

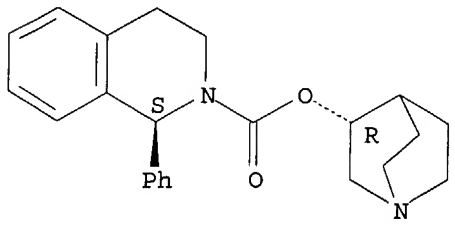


RN 242478-38-2 HCAPLUS
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

L14 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:827646 HCAPLUS
DN 136:145169
ED Entered STN: 14 Nov 2001
TI YM905, a novel M3 antagonist, inhibits Ca2+ signaling and c-fos gene expression mediated via muscarinic receptors in human T cells
AU Fujii, Takeshi; Kawashima, Koichiro
CS Department of Pharmacology, Kyoritsu College of Pharmacy, Minato-ku, Tokyo, 105-8512, Japan
SO General Pharmacology (**2000**), 35(2), 71-75
CODEN: GEPHDP; ISSN: 0306-3623
PB Elsevier Science Inc.
DT Journal
LA English
CC 1-12 (Pharmacology)
AB Our earlier observations suggest that M3 muscarinic acetylcholine (ACh) receptors (mAChRs) are involved in Ca2+ signaling and regulation of c-fos gene expression in T lymphocytes. Here, we describe the effects of YM905, a novel M3 antagonist, on evoked Ca2+ signaling and c-fos gene expression in CEM human leukemic T cells. YM905 significantly inhibited increases in intracellular free Ca2+ evoked by 10 μM oxotremorine-M, an M1/M3 agonist (IC50=100 nM), and also inhibited 10 μM oxotremorine-M-induced upregulation of c-fos gene expression at 1 μM. These findings demonstrate that YM905 antagonizes the intracellular responses in T cells induced via mAChRs, possibly M receptors.
ST muscarinic M3 antagonist YM905 calcium signaling cfos gene
IT Muscarinic antagonists
(M3; YM905 inhibits Ca2+ signaling and c-fos gene expression mediated via muscarinic receptors in human T cells)
IT Human
Signal transduction, biological
T cell (lymphocyte)
(YM905 inhibits Ca2+ signaling and c-fos gene expression mediated via muscarinic receptors in human T cells)
IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(c-fos; YM905 inhibits Ca2+ signaling and c-fos gene expression mediated via muscarinic receptors in human T cells)
IT Biological transport
(calcium; YM905 inhibits Ca2+ signaling and c-fos gene expression mediated via muscarinic receptors in human T cells)
IT **242478-38-2**, YM905
RL: PAC (Pharmacological activity); BIOL (Biological study)
(YM905 inhibits Ca2+ signaling and c-fos gene expression mediated via muscarinic receptors in human T cells)
IT 7440-70-2, Calcium, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(transport; YM905 inhibits Ca2+ signaling and c-fos gene expression mediated via muscarinic receptors in human T cells)
RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bany, U; J Neuroimmunol 1999, V97, P191 HCAPLUS
(2) Bonner, T; Neuron 1988, V1, P403 HCAPLUS
(3) Bonner, T; Science 1987, V237, P527 HCAPLUS
(4) Dong, G; J Pharmacol Exp Ther 1995, V274, P378 HCAPLUS
(5) Dorje, F; J Pharmacol Exp Ther 1991, V256, P727 MEDLINE
(6) Fujii, T; J Neuroimmunol 1998, V82, P101 HCAPLUS
(7) Fujii, T; J Neurosci Res 1996, V44, P66 HCAPLUS
(8) Fujii, T; Jpn J Pharmacol 2000, V84, P124 HCAPLUS
(9) Fujii, T; Naunyn-Schmiedeberg's Arch Pharmacol 2000, V362, P14 HCAPLUS
(10) Fujii, T; Neurosci Lett 1999, V259, P71 HCAPLUS
(11) Hoglund, A; J Pharmacol Exp Ther 1997, V281, P470 HCAPLUS

(12) Hulme, E; Annu Rev Pharmacol Toxicol 1990, V30, P633 HCAPLUS
(13) Illiano, G; Proc Natl Acad Sci USA 1973, V70, P2443 HCAPLUS
(14) Jakubik, J; Mol Pharmacol 1997, V52, P172 HCAPLUS
(15) Kaneda, T; Mol Pharmacol 1993, V43, P356 HCAPLUS
(16) Kawashima, K; Life Sci 1998, V62, P1701 HCAPLUS
(17) Kawashima, K; Pharmacol Ther 2000, V86, P29 HCAPLUS
(18) Kelly, L; J Biol Chem 1990, V265, P17657
(19) Maslinski, W; Brain Behav Immun 1989, V3, P1 MEDLINE
(20) Sato, K; Neurosci Lett 1999, V266, P17 HCAPLUS
(21) Strom, T; Proc Natl Acad Sci USA 1974, V71, P1330 HCAPLUS
(22) Tsien, R; Nature 1982, V295, P68 HCAPLUS
(23) Waelbroeck, M; Mol Pharmacol 1990, V38, P267 HCAPLUS

IT **242478-38-2**, YM905
RL: PAC (Pharmacological activity); BIOL (Biological study)
(YM905 inhibits Ca2+ signaling and c-fos gene expression mediated via muscarinic receptors in human T cells)

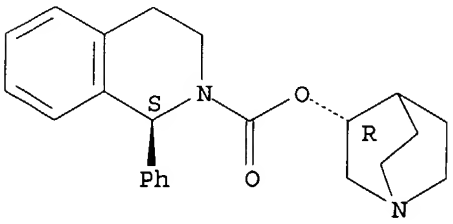
RN 242478-38-2 HCAPLUS

CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

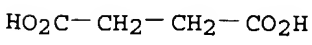
CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4



L14 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:552377 HCAPLUS
DN 135:313448
ED Entered STN: 31 Jul 2001
TI Effects of YM905, a novel muscarinic M3-receptor antagonist, on experimental models of bowel dysfunction in vivo
AU Kobayashi, Seiji; Ikeda, Ken; Suzuki, Mami; Yamada, Toshimitsu; Miyata, Keiji
CS Pharmacology Laboratories, Institute for Drug Discovery Research, Yamanouchi Pharmaceutical Co., Ltd., Tsukuba, 305-8585, Japan
SO Japanese Journal of Pharmacology (**2001**), 86(3), 281-288
CODEN: JJPAAZ; ISSN: 0021-5198
PB Japanese Pharmacological Society
DT Journal

LA English
CC 1-9 (Pharmacology)
AB We investigated the effects of YM905 [(+)-(1S,3'R)-quinuclidin-3'-yl 1-phenyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylate monosuccinate], a new orally active muscarinic M3-receptor antagonist, on bowel dysfunction in vivo using exptl. models that reproduce the symptoms present in irritable bowel syndrome (IBS). YM905 potently inhibited restraint stress-induced fecal pellet output in fed rats (ED50: 4.0 mg/kg) and diarrhea in fasted rats (ED50: 1.7 mg/kg), with similar potencies to the inhibition of bethanechol-, neostigmine- and nicotine-induced fecal pellet output in rats (ED50: 3.3, 7.9 and 4.5 mg/kg, resp.). YM905 also inhibited 5-hydroxytryptamine (5-HT)-, prostaglandin E2- and castor oil-induced secretory diarrhea in mice (ED50: 5.5, 14 and 6.3 mg/kg, resp.), but showed no significant effect on cholera toxin-induced intestinal secretion in mice. In addition, YM905 (3, 10 mg/kg) reversed morphine-decreased postprandial defecation in ferrets, a model of spastic constipation, whereas ramosetron, a 5-HT3-receptor antagonist, was not effective. The mode of YM905 action was similar to that of darifenacin, a selective M3-receptor antagonist, with equivalent potencies. By contrast, propantheline, an antimuscarinic drug that has been used for IBS, was much less potent. These results show that YM905 ameliorates a wide spectrum of bowel dysfunctions through the blockade of M3 receptors, suggesting its therapeutic potential for treating IBS.
ST muscarinic M3 receptor antagonist YM905 bowel dysfunction
IT Muscarinic antagonists
(M3; effects of YM905, a muscarinic M3-receptor antagonist, on exptl. models of bowel dysfunction)
IT Intestine, disease
(constipation; effects of YM905 on exptl. models of bowel dysfunction)
IT Antidiarrheals
(effects of YM905 on exptl. models of bowel dysfunction)
IT Intestine, disease
(irritable bowel syndrome; effects of YM905 on exptl. models of bowel dysfunction)
IT 298-50-0, Propantheline 133099-04-4, Darifenacin **242478-38-2**, YM 905
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of YM905 on exptl. models of bowel dysfunction)
RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Aggarwal, A; Gastroenterology 1994, V106, P945 MEDLINE
(2) Almy, T; Gastroenterology 1947, V8, P616
(3) Bueno, L; Baillieres Clin Gastroenterol 1988, V2, P123 MEDLINE
(4) Bueno, L; Eur J Pharmacol 1981, V75, P239 HCAPLUS
(5) Caulfield, M; Pharmacol Rev 1998, V50, P279 HCAPLUS
(6) de Ponti, F; J Pharmacol Exp Ther 1993, V264, P789 HCAPLUS
(7) Eglen, R; Pharmacol Rev 1996, V14, P531
(8) Ehlert, F; Life Sci 1997, V61, P1729 HCAPLUS
(9) Ferraz, A; Dig Dis Sci 1995, V40, P1417 HCAPLUS
(10) Honda, K; Jpn J Pharmacol 1993, V62, P43 HCAPLUS
(11) Humphrey, P; Aliment Pharmacol Ther 1999, V13(Suppl 2), P31
(12) Ikeda, K; FASEB J 1999, V13, PA157
(13) Kerr, P; Br J Pharmacol 1995, V115, P1518 HCAPLUS
(14) Miyata, K; Eur J Pharmacol 1993, V250, P303 HCAPLUS
(15) Miyata, K; J Pharmacol Exp Ther 1992, V261, P297 HCAPLUS
(16) Muraoka, M; Scand J Gastroenterol 1998, V33, P806 MEDLINE
(17) Nagakura, Y; Eur J Pharmacol 1997, V321, P53 HCAPLUS
(18) Nakayama, S; J Pharmacol Exp Ther 1990, V254, P792 HCAPLUS
(19) Nishiwaki, H; Jpn J Pharmacol 1998, V77, P271 HCAPLUS
(20) Ozaki, A; Jpn J Pharmacol 1999, V80, P93 HCAPLUS
(21) Pattee, P; Drugs 1992, V44, P200 MEDLINE

(22) Riviere, P; J Pharmacol Exp Ther 1991, V256, P547 HCAPLUS
(23) Shimizu, I; Arch Int Pharmacodyn Ther 1994, V328, P326 HCAPLUS
(24) Shook, J; J Pharmacol Exp Ther 1989, V251, P247 HCAPLUS
(25) Smart, H; Lancet 1987, V2, P475 MEDLINE
(26) Snape, W; Gastroenterology 1979, V77, P1235
(27) Snape, W; Gastroenterology 5th edition 1995, V2, P1619
(28) Taniyama, K; Gastroenterology 1991, V101, P1579 HCAPLUS
(29) Thompson, W; Gut 1984, V25, P305 MEDLINE
(30) Wallis, R; Life Sci 1999, V64, P395 HCAPLUS
(31) Williams, C; Gastroenterology 1988, V94, P611 MEDLINE

IT **242478-38-2**, YM 905
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of YM905 on exptl. models of bowel dysfunction)

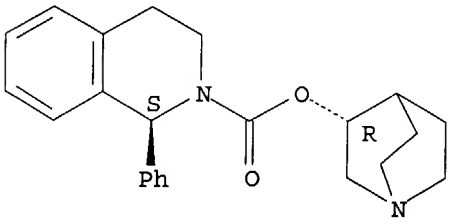
RN 242478-38-2 HCAPLUS

CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

L14 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:451981 HCAPLUS
DN 133:317043
ED Entered STN: 05 Jul 2000
TI YM-905 (Yamanouchi Pharmaceutical Co Ltd)
AU Heading, Christine E.
CS Open University, Ruislip, HA4 7DD, UK
SO Current Opinion in Central & Peripheral Nervous System Investigational Drugs (**2000**), 2(3), 321-325
CODEN: COCDFA; ISSN: 1464-844X
PB PharmaPress Ltd.
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review with 23 refs. Yamanouchi is developing YM-905, a selective M3

muscarinic receptor antagonist, as a potential treatment for urinary incontinence and irritable bowel syndrome (IBS). It is in phase II trials in the US and Europe as a potential treatment for urinary incontinence and in phase I trials in Japan for IBS. Launch in the US and European markets is expected between 2003 and 2005. The drug shows a high affinity for the M3 receptor (Ki = 12 nM in rats) and effectively inhibits rhythmic bladder contractions without the common atropinic side effects such as dry mouth in humans. In preclin. studies, YM-905 (the succinate salt of the same free base of which YM-53705 is the monochloride salt) potently and competitively inhibited carbachol-induced contractions of guinea pig colon, with a pA2 value of 7.5. It was also shown to inhibit restraint stress-induced defecation and diarrhea over a dose range of 1-30 mg/kg. Preclin. studies have demonstrated that YM-53705 inhibited an increase in calcium and upregulated c-fos gene expression in a human T-cell line stimulated with oxotremorine. It has been suggested that YM-53705 modulates T-cell function via M3 receptors.

ST review YM 905 pharmacol bladder incontinence irritable bowel syndrome

IT Bladder
(incontinence; YM 905 pharmacol. for treatment of urinary incontinence and irritable bowel syndrome)

IT Intestine, disease
(irritable bowel syndrome; YM 905 pharmacol. for treatment of urinary incontinence and irritable bowel syndrome)

IT **242478-38-2P**, YM 905
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(pharmacol. of YM 905 for treatment of urinary incontinence and irritable bowel syndrome)

RE.CNT 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) ABN AMRO; Analyst Report 1999
(2) Anon; Pharma Jpn 1998, V1609
(3) Anon; Pharma Jpn 1998, V1596, P15
(4) Anon; Pharma Jpn 1999, V1631, P1
(5) Anon; Pharma Jpn 1999, V1667, P2
(6) Anon; SCRIP 1997, V2290, P16
(7) Eglen, R; Curr Opin Chem Biol 1999, V3(3), P426
(8) Holobowski, M; IDrugs 1998, V1(7), P747
(9) Ikeda, K; FASEB J 1999, V13(4), PA157
(10) Ikeda, K; Jpn J Pharmacol 1998, V76(suppl 1)
(11) Kobayshi, S; FASEB J 1999, V13(5), PA807
(12) Lehman Brothers; Analyst Report 1999
(13) Lehman Brothers; Analyst Report 1999
(14) Mealy, M; Drugs Future 1999, V24(8), P871
(15) Scribabine, A; Cardiovasc Drug Rev 1999, V17(2), P192
(16) Suzuki, M; Jpn J Pharmacol 1998, V76(suppl 1)
(17) Takeshi, F; Jpn J Pharmacol 2000, V82(1), P0
(18) Takeuchi, M; ACS 1997
(19) Wright, T; IDDB Meeting Report 1998
(20) Wright, T; IDDB Meeting Report 2000
(21) Yamanouchi Pharmaceutical; Annual Report 1998
(22) Yamanouchi Pharmaceutical Co Ltd; Annual Report 1999
(23) Yamanouchi Pharmaceutical Co Ltd; Company World Wide Web Site 1999

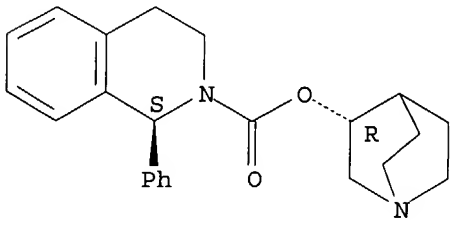
IT **242478-38-2P**, YM 905
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(pharmacol. of YM 905 for treatment of urinary incontinence and

irritable bowel syndrome)
RN 242478-38-2 HCAPLUS
CN Butanedioic acid, compd. with (1S)-(3R)-1-azabicyclo[2.2.2]oct-3-yl 3,4-dihydro-1-phenyl-2(1H)-isoquinolinecarboxylate (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 242478-37-1
CMF C23 H26 N2 O2

Absolute stereochemistry. Rotation (+).



CM 2

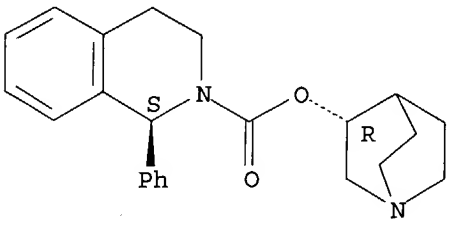
CRN 110-15-6
CMF C4 H6 O4

$HO_2C-CH_2-CH_2-CO_2H$

L14 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:433740 HCAPLUS
DN 133:317413
ED Entered STN: 29 Jun 2000
TI Gastric cytoprotective activity of ilicic aldehyde in rats and mice
AU Donadel, O. J.; Maria, A.; Wendel, G.; Guerreiro, E.; Giordano, O.
CS Quimica Organica, INTEQUI-CONICET, Argent.
SO Molecules [Electronic Publication] (2000), 5(3), 462-464
CODEN: MOLEFW; ISSN: 1420-3049
URL: http://www.mdpi.org/molecules/papers/50300252.pdf
PB Molecular Diversity Preservation International
DT Journal; (online computer file)
LA English
CC 1-9 (Pharmacology)
AB Ilicic alc., a natural sesquiterpene, was previously converted to its aldehyde by Jones' oxidation The aldehyde prevented the formation of gastric mucosal lesions induced by EtOH and other necrotizing agents in mice and rats.
ST ilicic aldehyde stomach cytoprotectant; gastroprotectant ilicic aldehyde
IT Antiulcer agents
(ilicic aldehyde cytoprotective activity as)
IT Cytoprotective agents
(ilicic aldehyde gastric cytoprotective activity)
IT Stomach, disease
(mucosa, injury; ilicic aldehyde cytoprotective activity against)
IT Stomach, disease
(ulcer; ilicic aldehyde cytoprotective activity against)
IT **242478-37-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastric cytoprotective activity of ilicic aldehyde)
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) De Lean, A; Lab of Theoretical and Physical Biology 1988
(2) Donadel, O; IV Simposio Internacional de Quimica de Productos Naturales y sus Aplicaciones
(3) Guerreiro, E; Phytochemistry 1979, V18, P1235 HCAPLUS
(4) Marazzi-Uberti, E; Med Exp 1961, V4, P284
(5) Robert, A; Gastroenterology 1979, V77, P433 HCAPLUS
(6) Rodriguez, A; J Med Chem 1997, V40(12), P1827 HCAPLUS
(7) Yamasaki, K; Japan J Pharmacol 1989, V49, P441 HCAPLUS
IT **242478-37-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gastric cytoprotective activity of ilicic aldehyde)
RN 242478-37-1 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

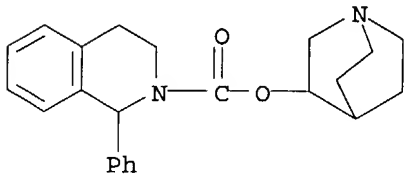


L14 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:731705 HCAPLUS
DN 132:202452
ED Entered STN: 17 Nov 1999
TI YM-905: treatment of urinary incontinence, muscarinic M3 antagonist
AU Mealy, N.; Castaner, J.
CS Prous Science, Barcelona, 08080, Spain
SO Drugs of the Future (**1999**), 24(8), 871-874
CODEN: DRFUD4; ISSN: 0377-8282
PB Prous Science
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review, with 7 refs., discussing the synthesis and the pharmacol. actions of the title compound
ST review YM 905 muscarinic antagonist bladder incontinence
IT Muscarinic antagonists
(M3; YM-905: treatment of urinary incontinence, muscarinic M3 antagonist)
IT Bladder
(incontinence; YM-905: treatment of urinary incontinence, muscarinic M3 antagonist)
IT **180272-15-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(YM-905: treatment of urinary incontinence, muscarinic M3 antagonist)
RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Anon; WO 9620194 HCAPLUS
(2) Ikeda, K; FASEB J 1999, V13(4, Part 1)
(3) Ikeda, K; Jpn J Pharmacol 1998, V76(Suppl 1)
(4) Kobayashi, S; FASEB J 1999, V13(5, Part 2)
(5) Suzuki, M; Jpn J Pharmacol 1998, V76(Suppl 1)
(6) Takeuchi, M; EP 801067 HCAPLUS
(7) Takeuchi, M; 213th ACS Natl Meet 1997
(8) Yamanouchi Pharmaceutical Co, Ltd; YM-905 development status 1999
IT **180272-15-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(YM-905: treatment of urinary incontinence, muscarinic M3 antagonist)
RN 180272-15-5 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)

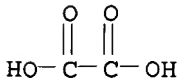
CM 1

CRN 180272-14-4
CMF C23 H26 N2 O2



CM 2

CRN 144-62-7
CMF C2 H2 O4



L14 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:35996 HCAPLUS
DN 128:114881
ED Entered STN: 22 Jan 1998
TI Preparation of quinuclidine-containing isoquinolines and muscarine M3 receptor antagonists containing them
IN Naito, Ryo; Takeuchi, Makoto; Okamoto, Yoshinori; Ikeda, Masaru; Isomura, Yasuo
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC ICM C07D453-02
ICS A61K031-47
CC 27-20 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 1

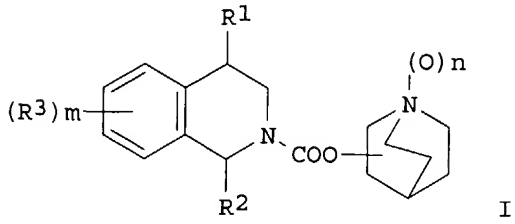
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 10007675	A2	19980113	JP 1996-162221	19960621 <--
PRAI JP 1996-162221		19960621 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
JP 10007675	ICM	C07D453-02
	ICS	A61K031-47

OS MARPAT 128:114881

GI



I

AB Isoquinolines I (R1 = OH, lower alkoxy, lower alkyl; R2 = aryl, cycloalkyl, heterocyclyl; R3 = halo, OH, lower alkoxy, CO2H, lower alkoxycarbonyl, lower acyl, etc.; m = 0-3; n = 0, 1) or their salts, useful as muscarine M3 receptor antagonists, are prepared (±)-Trans-1-phenyl-1,2,3,4-tetrahydro-4-isoquinolinol (0.28 g) was treated with 0.28 g (3R)-3-quinuclidinyl chloroformate.HCl at room temperature for 2.5 h to give 0.15 g trans-(1S,3'R,4S)- and trans-(1R,3'R,4R)-I (R1 = OH, R2 = Ph, R3 = H, n = 0). I was tested for in vitro muscarine receptor affinity and in vivo antagonistic activity.

ST quinuclidine isoquinoline prepn muscarine antagonist; muscarine M3 antagonist quinuclidine isoquinoline

IT Muscarinic antagonists
(M3; preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor antagonists)

IT Bronchi
(chronic bronchitis, inhibition; preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor antagonists)

IT Lung, disease
(chronic obstructive, inhibition; preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor antagonists)

IT Bladder
(incontinence, inhibition; preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor antagonists)

IT Antiasthmatics
(preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor antagonists)

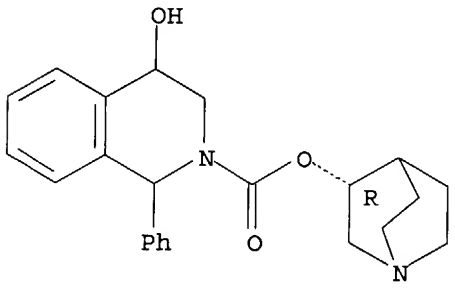
IT Nose
(rhinitis, inhibition; preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor antagonists)

IT Urinary tract
(urinary frequency, inhibition; preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor antagonists)

IT **201660-36-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor
antagonists)
IT 90861-84-0 90861-85-1 201660-37-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor
antagonists)
IT **201660-36-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinuclidine-containing isoquinolines as muscarine M3 receptor
antagonists)
RN 201660-36-8 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-4-hydroxy-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, [2(R)]-[partial]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:516723 HCAPLUS
DN 125:167804
ED Entered STN: 29 Aug 1996
TI Preparation of new quinuclidine derivatives as muscarinic M3 receptor antagonists
IN Takeuchi, Makoto; Naito, Ryo; Hayakawa, Masahiko; Okamoto, Yoshinori; Yonetoku, Yasuhiro; Ikeda, Ken; Isomura, Yasuo
PA Yamanouchi Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
IC ICM C07D453-02
ICS A61K031-435
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9620194	A1	19960704	WO 1995-JP2713	19951227 <--

W: AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

CA 2208839	AA	19960704	CA 1995-2208839	19951227	<--
AU 9643553	A1	19960719	AU 1996-43553	19951227	<--
AU 695616	B2	19980820			
EP 801067	A1	19971015	EP 1995-942276	19951227	<--
EP 801067	B1	20030305			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE					
CN 1171109	A	19980121	CN 1995-197088	19951227	<--
CN 1045601	B	19991013			
HU 77006	A2	19980302	HU 1997-1895	19951227	<--
RU 2143432	C1	19991227	RU 1997-112907	19951227	<--
JP 3014457	B2	20000228	JP 1996-520367	19951227	<--
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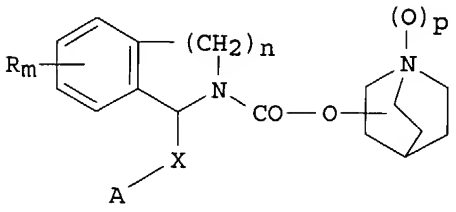
PL 182344	B1	20011231	PL 1995-321019	19951227	<--
AT 233761	E	20030315	AT 1995-942276	19951227	<--
PT 801067	T	20030731	PT 1995-942276	19951227	<--
ES 2193208	T3	20031101	ES 1995-942276	19951227	<--
FI 9702775	A	19970822	FI 1997-2775	19970627	<--
NO 9703027	A	19970828	NO 1997-3027	19970627	<--
US 6017927	A	20000125	US 1997-860377	19970828	<--
US 6174896	B1	20010116	US 1999-312392	19990514	<--
PRAI JP 1994-327045	A	19941228	<--		
JP 1996-520367	A3	19951227	<--		
WO 1995-JP2713	W	19951227	<--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 9620194	ICM	C07D453-02	
	ICS	A61K031-435	
US 6017927	ECLA	C07D453/02	<--
US 6174896	ECLA	C07D453/02	<--

OS MARPAT 125:167804

GI



I

AB Quinuclidine derivs. I [ring A = optionally substituted aryl, cycloalkyl, cycloalkenyl, heteroaryl containing 1 to 4 heteroatoms selected from among oxygen, nitrogen and sulfur, or 5- to 7-membered saturated heterocycle; X = single bond or methylene; R = halo, hydroxy, lower alkoxy, carboxy, lower alkoxycarbonyl, lower acyl, mercapto, lower alkylthio, sulfonyl, lower alkylsulfonyl, sulfinyl, lower alkylsulfinyl, sulfonamido, lower alkanesulfonamido, carbamoyl, thio-carbamoyl, mono- or di(lower alkyl)carbamoyl, nitro, cyano, amino, mono- or di(lower alkyl)amino, methylenedioxy, ethylenedioxy or lower alkyl optionally substituted by halogeno, hydroxy, lower alkoxy, amino or mono- or di(lower alkyl)amino; p = 0 or 1; m = integer of 1 to 3; n = integer of 1 or 2], their salts, N-oxides, or quaternary ammonium salts, having an antagonistic effect on muscarinic M3 receptors and are useful as a preventive or remedy for urol. diseases, respiratory diseases or digestive diseases, are prepared Thus, Et 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate (preparation given) was reacted with 3-quinuclidinol in toluene containing NaH at 140° for 2 days to give the title compound 3-quinuclidinyl 1-phenyl-1,2,3,4-tetrahydro-2-isoquinolinecarboxylate isolated as the oxalate salt. In an in vitro study, I had Ki values of 10-3 to 10-10 M against muscarinic M3 receptors.

ST quinuclidine deriv prepn antagonist muscarinic receptor; muscarinic M receptor antagonist quinuclidine deriv

IT Digestive tract
Urinary tract
(disease, disorder; preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)

IT Respiratory tract
(disease, preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)

IT Receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(muscarinic M3, preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)

IT **180272-14-4P 180272-15-5P 180272-16-6P**
180272-17-7P 180272-19-9P 180272-20-2P 180272-21-3P
180272-23-5P 180272-24-6P 180272-25-7P
180272-26-8P **180272-27-9P 180272-28-0P**
180272-29-1P 180272-30-4P **180468-37-5P**
180468-38-6P 180468-39-7P 180468-40-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)

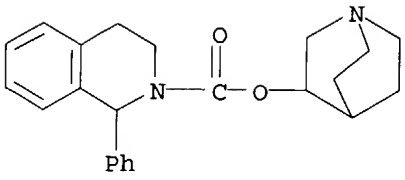
IT 79-22-1, Methyl chloroformate 541-41-3, Ethyl chloroformate 1619-34-7, 3-Quinuclidinol 19716-56-4, 1-Benzyl-1,2,3,4-tetrahydroisoquinoline 22990-19-8, 1-Phenyl-1,2,3,4-tetrahydroisoquinoline 25333-42-0 34583-34-1 35392-51-9 87443-64-9, 1-Cyclohexyl-1,2,3,4-tetrahydroisoquinoline 112891-30-2 112891-31-3 118864-75-8 120086-34-2 120086-35-3 135675-29-5 180272-43-9 180272-44-0 180272-45-1 180272-46-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)

IT 180272-31-5P 180272-32-6P 180272-33-7P 180272-34-8P 180272-35-9P 180272-36-0P 180272-37-1P 180272-38-2P 180272-39-3P 180272-40-6P 180272-41-7P 180272-42-8P 180468-41-1P 180468-42-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)

IT **180272-14-4P 180272-15-5P 180272-16-6P**
180272-23-5P 180272-24-6P 180272-25-7P
180272-27-9P 180272-28-0P 180272-29-1P
180468-37-5P 180468-38-6P 180468-39-7P
180468-40-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of new quinuclidine derivs. as muscarinic M3 receptor antagonists)

RN 180272-14-4 HCAPLUS

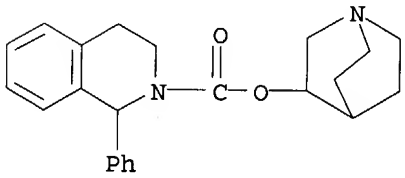
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-15-5 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, ethanedioate (1:1) (9CI) (CA INDEX NAME)

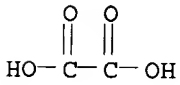
CM 1

CRN 180272-14-4
CMF C23 H26 N2 O2

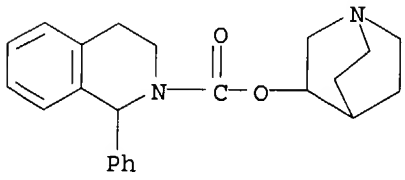


CM 2

CRN 144-62-7
CMF C2 H2 O4



RN 180272-16-6 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride (9CI) (CA INDEX NAME)

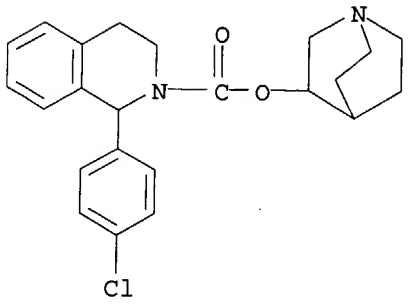


● HCl

RN 180272-23-5 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-chlorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

CM 1

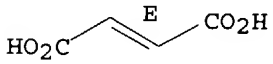
CRN 180272-22-4
CMF C23 H25 Cl N2 O2



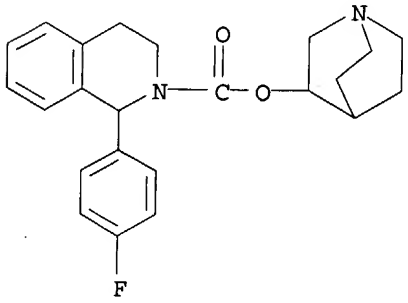
CM 2

CRN 110-17-8
CMF C4 H4 O4

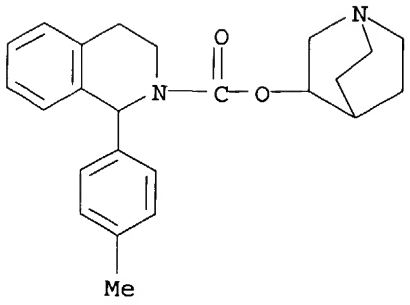
Double bond geometry as shown.



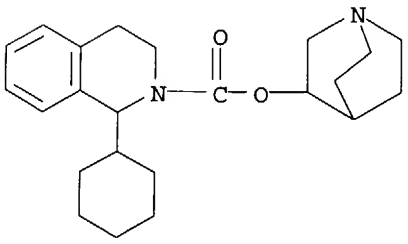
RN 180272-24-6 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 1-(4-fluorophenyl)-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



RN 180272-25-7 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-(4-methylphenyl)-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)

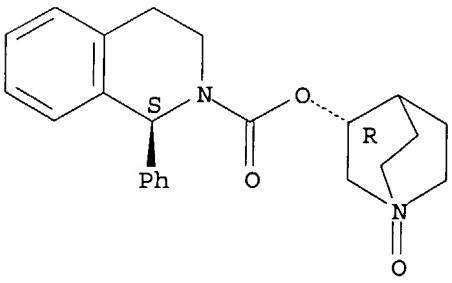


RN 180272-27-9 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 1-cyclohexyl-3,4-dihydro-, 1-azabicyclo[2.2.2]oct-3-yl ester (9CI) (CA INDEX NAME)



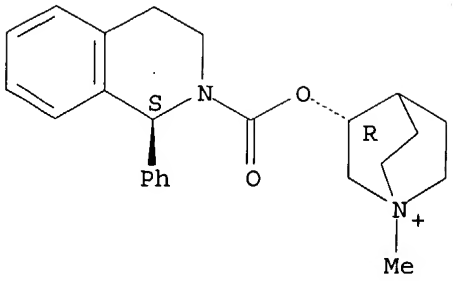
RN 180272-28-0 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, (3R)-1-oxido-1-azabicyclo[2.2.2]oct-3-yl ester, (1S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 180272-29-1 HCAPLUS
CN 1-Azoniabicyclo[2.2.2]octane, 3-[[[(1S)-3,4-dihydro-1-phenyl-2(1H)-isoquinolinyl]carbonyl]oxy]-1-methyl-, iodide, (3R)- (9CI) (CA INDEX NAME)

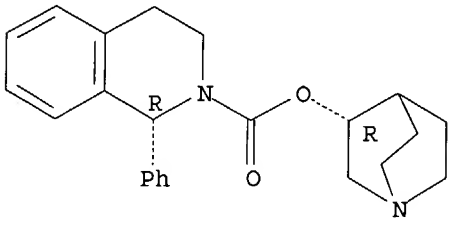
Absolute stereochemistry.



● I^-

RN 180468-37-5 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R*,R*)]- (9CI) (CA INDEX NAME)

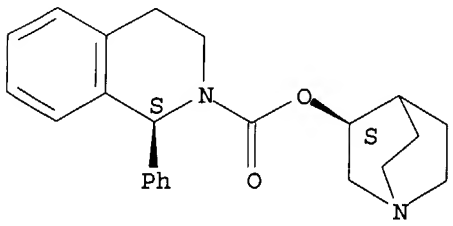
Absolute stereochemistry. Rotation (-).



● HCl

RN 180468-38-6 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

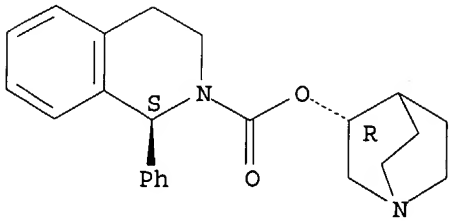
Absolute stereochemistry. Rotation (+).



● HCl

RN 180468-39-7 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

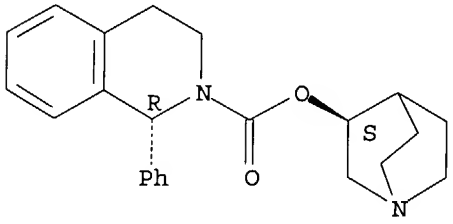
Absolute stereochemistry. Rotation (+).



● HCl

RN 180468-40-0 HCAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-1-phenyl-, 1-azabicyclo[2.2.2]oct-3-yl ester, monohydrochloride, [S-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● HCl

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